

# Super-Selective Adrenal Venous Sampling: A Diagnostic Tool when Planned, but a Liability when Incidental

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## AUTHORS' CONTRIBUTIONS

Contributions to this case report were distributed amongst the 4 authors proportionally with regards to performing the procedures, researching the topic of discussion, and writing & editing of the manuscript.

## DISCLOSURES

The authors declare that there are no conflicts of interest regarding the publication of this article.

## CONSENT

Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

## HUMAN AND ANIMAL RIGHTS

Not Applicable.

## Background

This case illustrates a technical pitfall of unintentional super-selective adrenal venous sampling and offers practical guidance on tributary selection strategy during AVS. An apparently unreported right adrenal venous variant encountered during the procedure is also described.

## CASE REPORT

### ABSTRACT

Adrenal vein sampling (AVS) is considered the gold standard for differentiating unilateral from bilateral primary aldosteronism (PA). However, technical and anatomic factors may complicate interpretation. One such factor is the recognition of adrenal venous tributaries, as individual branches may carry markedly different aldosterone concentrations. We report the case of an unintended super-selective sampling on repeat AVS that resulted in a nondiagnostic selectivity index (SI) and thus an inconclusive study.

### Clinical Presentation

A 55-year-old female with a history of long-standing hypertension was incidentally noted to have a 2 x 1.7 cm right adrenal nodule on abdominal CT, suspicious for adrenal adenoma. Her symptoms included hypertension and recurrent headaches, without hypokalemia or other abnormal baseline biochemical values – an increasingly common presentation of PA. Laboratory studies confirmed the diagnosis of PA with an elevated aldosterone-renin ratio of 75.4 (Aldosterone concentration of 12.6 ng/dL and Renin activity of <0.167 ng/mL/hr). She was referred to interventional radiology for AVS to differentiate between unilateral versus bilateral hyperaldosteronism. The initial study was technically successful, however, conflicted with the CT

findings. A second AVS was conducted three months later but was unsuccessful due to super-selective sampling of a right adrenal vein tributary, resulting in a nondiagnostic SI.

### Procedure

ACTH stimulation was used as an IV bolus injection of 0.25 mg 30 minutes prior to the procedure start. Dual right-sided femoral vein access was achieved for selective and simultaneous, bilateral adrenal sampling using 5 French Glidecath catheters. Venograms of the inferior vena cava (IVC) and left renal vein were obtained to identify the origin of the adrenal veins. Notably, the right adrenal vein courses laterally from the gland and joins the IVC medially – a rare, apparently unreported presentation in the available literature (Figures 1,2).

**First procedure:** Both adrenal veins were cannulated successfully. Cortisol enrichment confirmed selectivity, with an SI of 7.92 on the right and 4.46 on the left. Aldosterone-to-cortisol ratios (A/C) were 2.36 on the right and 2.0 on the left, resulting in a lateralization index (LI) of 1.18. These results indicated technically successful AVS without evidence of lateralization, suggestive of bilateral aldosterone hypersecretion. This finding was inconsistent with the CT finding, however, and a repeat AVS was planned.

**Second procedure:** The left adrenal vein was again selectively cannulated and two samples were obtained with results consistent with the first procedure (SI of 4.54 and 5.4). On the right side, multiple cannulation attempts of the previously sampled inferior tributary were unsuccessful, possibly due to prior instrumentation, and thus the previously non-cannulated superior tributary was selected. Three samples were obtained from the superior branch to improve sampling reliability; however, all were non-diagnostic due to insufficient cortisol levels (SI of 0.92, 0.91 and 0.98).

### Findings and Interpretation

The first procedure yielded a technically successful and interpretable result, with bilateral hypersecretion suggested by the LI. The discordance with CT imaging, rather than any procedural failure, prompted repeat AVS.

The most significant finding of the second procedure was the failure to obtain diagnostic cortisol levels from the right superior adrenal tributary. This finding may suggest that the hypersecreting portion of the right adrenal gland is selectively drained by the inferior tributary.

Overall, the selective cannulation of different adrenal tributaries can either complicate or support interpretation, depending on the operator's knowledge and intention of such selections. This case illustrates how preferential drainage may alter AVS interpretation and underscores the importance of preoperative planning with regards to selection approach – whether to sample multiple tributaries for enhanced diagnostic accuracy (known as super-selective AVS) or to sample from the main adrenal vein or a specific tributary due to imaging context. The operator must be informed of these nuances as incomplete AVS interpretations may inappropriately direct patients toward unnecessary adrenalectomy.

## DISCUSSION

### Indication for AVS

Primary aldosteronism (PA) accounts for up to 10% of cases of hypertensive patients [1]. AVS is the recommended method for differentiating between a unilateral aldosterone-producing adenoma (APA) and bilateral idiopathic hyperaldosteronism (IHA) [2]. Differentiation is important to direct management, as APA is managed surgically while IHA is managed medically.

### Clinical and Imaging Findings

In the reported case, a patient with long-standing history of hypertension was incidentally found to have a right-sided adrenal mass on abdominal CT. After laboratory tests confirmed PA, AVS was conducted to differentiate between a unilateral APA versus bilateral IHA. AVS results were suggestive of IHA, and thus the patient continued medical management rather than adrenalectomy. However, since CT findings were suggestive of a unilateral adrenal adenoma, a repeat AVS was conducted.

The second procedure revealed a superior right adrenal venous tributary (Figure 2) which was not appreciated during the first procedure (Figure 1). Selective cannulation and sampling of the superior tributary were completed but deemed nondiagnostic due to an SI less than 3. This pattern is consistent with apparent aldosterone suppression, a phenomenon previously described in the setting of unintended super-selective sampling [3].

Notably, the venograms demonstrated a right adrenal vein exiting the gland laterally and joining the IVC from its medial side. This variant anatomy is not described in the literature to the authors' knowledge and represents a rare venous variant that may complicate AVS or other adrenal procedures. In our case, it did not significantly complicate the AVS but was noted to be unusual.

### Treatment and Prognosis

Without definitive lateralization, our patient was managed medically by transitioning her antihypertensive medication to a mineralocorticoid receptor antagonist. This aligns with the recommended guidelines of the Endocrine Society, which recommends surgical resection only when AVS demonstrates a clear unilateral disease [2]. Patients with untreated PA have disproportionate end organ dysfunction when compared to age- and sex-matched controls with essential hypertension at similar blood pressures [2]. Treatment with mineralocorticoid receptor antagonists or unilateral adrenalectomy for IHA or APA, respectively, significantly improves mortality and morbidity.

### Literature Context

The available literature underscores the importance of super-selective AVS when a primary AVS study is nondiagnostic. DePietro et al. highlight the importance of selective sampling from multiple adrenal venous tributaries since there may be several causes of apparent aldosterone suppression, including variant or selective APA drainage, sampling during the quiescent phase of aldosterone secretion, and sampling error including but not limited to incidental super-selective sampling [3]. Our case demonstrated the opposite, where the primary AVS was diagnostic and the second, super-selective case was not. This supports one of DePietro et al.'s claims of selective APA drainage resulting in apparent aldosterone suppression and highlights the importance of strategic, comprehensive venous selections during super-selective AVS.

Regarding variant anatomy, a retrospective review by Scholten et al. included 546 consecutive laparoscopic adrenalectomies in 506 patients. In these cases, variant anatomy was observed in 70 (13%) patients, with anatomical variations being more common on the right side (17% vs 9% on the left side) [4]. These variants included no identifiable main adrenal vein, 1 adrenal vein with additional small veins, 2 or more adrenal veins, and variant adrenal vein drainage into the hepatic vein - there was no mention of a medially coursing adrenal vein relative to the IVC as seen in our case. Chan et al. recognized

the challenges associated with correctly identifying and successfully cannulating the adrenal veins. They recommended a late arterial phase imaging computed tomography (CT) to identify variant venous anatomy before AVS [5].

#### TEACHING POINT

Super-selective AVS is a recognized technique to enhance diagnostic accuracy. However, it may also complicate laboratory interpretation if done unintentionally or without sampling all relevant tributaries, as it can suggest apparent aldosterone suppression. This phenomenon can be seen when selecting a branch that does not drain a hypersecreting nodule in the context of an APA. If preprocedural imaging confidently delineates APA venous drainage, intentional super-selective AVS may be completed. Otherwise, the authors recommend sampling from the main adrenal vein, if there is normal anatomy, and waiting for laboratory confirmation of a diagnostic SI before withdrawing access and concluding the procedure. If the SI returns nondiagnostic, or if there is variant anatomy with multiple adrenal veins, the authors recommend proceeding with selective cannulation of all tributaries to compare aldosterone secretion activity across the entire adrenal gland.

#### QUESTIONS

**Question 1:** Which of the following statements regarding adrenal venous anatomy and AVS is correct?

1. A duplicated adrenal vein is a common finding.
2. A duplicated adrenal vein can complicate AVS interpretation. (applies)
3. Unidentified anatomic variants of adrenal venous drainage may alter treatment decisions. (applies)
4. Variant left adrenal vein anatomy is more common than variant right-sided anatomy.
5. Failure to recognize venous variants has no effect on diagnostic accuracy.
  1. A duplicated adrenal vein is a rare finding. [variant anatomy was observed in 70 (13%) patients, with anatomical variations being more common on the right side (17% vs 9% on the left side). These variants included... 2 or more adrenal veins...].
  2. An unidentified duplicated adrenal vein, or other variant anatomy, may complicate AVS interpretation. [...there may be several causes of apparent aldosterone suppression, including variant or selective APA drainage].
  3. If unidentified, variant adrenal venous drainage may alter interpretation, in turn altering treatment decisions. [The operator must be informed of these nuances as incomplete AVS interpretations may inappropriately direct patients toward unnecessary adrenalectomy].
  4. Variant right sided adrenal vein anatomy is rare, but more common than the left side. [In a retrospective review of 546 laparoscopic adrenalectomies, variant anatomy was observed in 70 (13%) patients, with anatomical variations being more common on the right side].
  5. Variant adrenal venous anatomy may affect diagnostic accuracy. [Chan et al. recognized the challenges associated with

correctly identifying and successfully cannulating the adrenal veins].

**Question 2:** In the reported case, why were the results of the second adrenal vein sampling considered non-diagnostic?

1. Only the left adrenal vein was successfully cannulated.
2. The SI value of the right adrenal sample was less than 3. (applies)
3. Samples from the right superior tributary had insufficient cortisol levels. (applies)
4. The left adrenal vein showed no cortisol enrichment.
5. The patient had bilateral adrenal adenomas.
  1. Both adrenal veins were successfully sampled in the first procedure, and the left adrenal vein was again successfully sampled in the second. [The left adrenal vein was again selectively sampled with results consistent with the first procedure].
  2. It is generally accepted that an SI  $\geq 5$  is necessary for a positive AVS, but some centers will accept values  $\geq 3$  ( $\geq 2$  if done without ACTH stimulation). [Selective cannulation and sampling of the superior tributary were completed but deemed nondiagnostic due to an SI less than 3].
  3. Samples from the right superior branch yielded insufficient cortisol, making them non-diagnostic. [Three samples were obtained from the superior branch to improve sampling reliability; however, all were non-diagnostic due to insufficient cortisol levels (SI of 0.92, 0.91 and 0.98)].
  4. Cortisol enrichment confirmed selectivity in the left adrenal vein. [The left adrenal vein was again selectively sampled with results consistent with the first procedure].
  5. There was no evidence of bilateral adrenal adenomas in this patient. [...was incidentally noted to have a 2 x 1.7 cm right adrenal nodule on abdominal CT, suspicious for adrenal adenoma].

**Question 3:** What is the gold standard method for differentiating unilateral from bilateral primary hyperaldosteronism?

1. Adrenal CT imaging
2. Adrenal venous sampling (applies)
3. Serum aldosterone-to-renin ratio
4. PET-CT imaging
5. MRI of the adrenal glands
  1. Adrenal CT imaging does not provide information on laterality of primary aldosteronism. [Adrenal vein sampling (AVS) is considered the gold standard for differentiating unilateral from bilateral primary hyperaldosteronism].
  2. AVS is the gold standard study for lateralization of primary hyperaldosteronism. [Adrenal vein sampling (AVS) is considered the gold standard for differentiating unilateral from bilateral primary hyperaldosteronism].
  3. Serum aldosterone-to-renin ratio provides information on the presence of primary hyperaldosteronism, but not on its laterality. [Adrenal vein sampling (AVS) is considered the gold standard for differentiating unilateral from bilateral primary hyperaldosteronism].

4. PET-CT imaging does not provide information on laterality of primary aldosteronism. [Adrenal vein sampling (AVS) is considered the gold standard for differentiating unilateral from bilateral primary hyperaldosteronism].

5. MRI of the adrenal glands does not provide information on laterality of primary aldosteronism. [Adrenal vein sampling (AVS) is considered the gold standard for differentiating unilateral from bilateral primary hyperaldosteronism].

**Question 4:** Which of the following are recognized causes of inconclusive or non-diagnostic adrenal vein sampling?

1. Operator error (applies)
2. Anatomical adrenal venous variants (applies)
3. Sampling during the quiescent phase of aldosterone secretion (applies)
4. Elevated serum potassium levels
5. Super-selective sampling of a non-draining adrenal vein (applies)

1. As is any procedure, operator error can lead to a nondiagnostic study. [...there may be several causes of apparent aldosterone suppression, including... sampling error...].

2. Anatomical variants may complicate AVS interpretation. [...there may be several causes of apparent aldosterone suppression, including variant or selective APA drainage...].

3. Sampling during the quiescent phase is another cause of inconclusive results. [...there may be several causes of apparent aldosterone suppression, including... sampling during the quiescent phase of aldosterone secretion...].

4. Elevated serum potassium is not a reported cause of nondiagnostic AVS. Hypokalemia, not hyperkalemia, is associated with primary aldosteronism.

5. Super-selective sampling of an adrenal vein tributary that does not drain the hypersecreting segment of the adrenal gland leads to a nondiagnostic study. [...there may be several causes of apparent aldosterone suppression, including... incidental super-selective sampling].

**Question 5:** Which of the following management principles aligns with the Endocrine Society guidelines for primary hyperaldosteronism?

1. Surgical adrenalectomy is recommended for all patients with resistant hypertension.
2. Surgical adrenalectomy is appropriate only when AVS demonstrates unilateral disease. (applies)
3. Medical therapy is never appropriate in primary hyperaldosteronism.
4. Imaging alone is sufficient to guide surgical decision-making.
5. Medical therapy is appropriate in primary hyperaldosteronism when AVS demonstrates bilateral disease. (applies)

1. Surgery is not offered to all resistant hypertensive patients, but specifically to those with AVS-proven unilateral disease. [This aligns with the recommended guidelines of the Endocrine Society, which recommends surgical resection only when AVS demonstrates a clear unilateral disease].

2. Adrenalectomy is indicated when AVS confirms unilateral aldosterone-producing adenoma, as surgical resection can be curative. [APA is managed surgically, while IHA is managed medically].

3. Medical therapy is an important option in patients with bilateral disease or indeterminate AVS. [... IHA is managed medically].

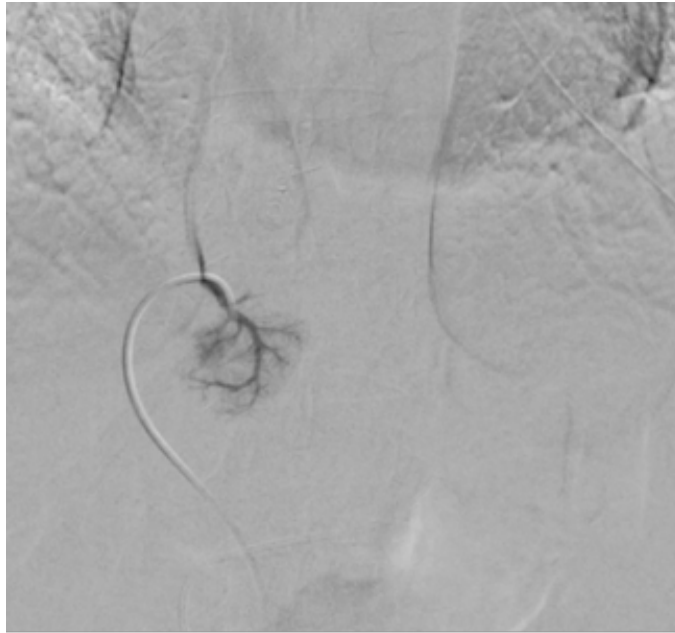
4. Imaging alone is insufficient, since CT and MRI cannot reliably determine laterality; AVS remains the gold standard. [Adrenal vein sampling (AVS) is considered the gold standard for differentiating unilateral from bilateral primary hyperaldosteronism].

5. Medical therapy is the standard of care when AVS suggests bilateral disease or fails to demonstrate lateralization. [APA is managed surgically, while IHA is managed medically].

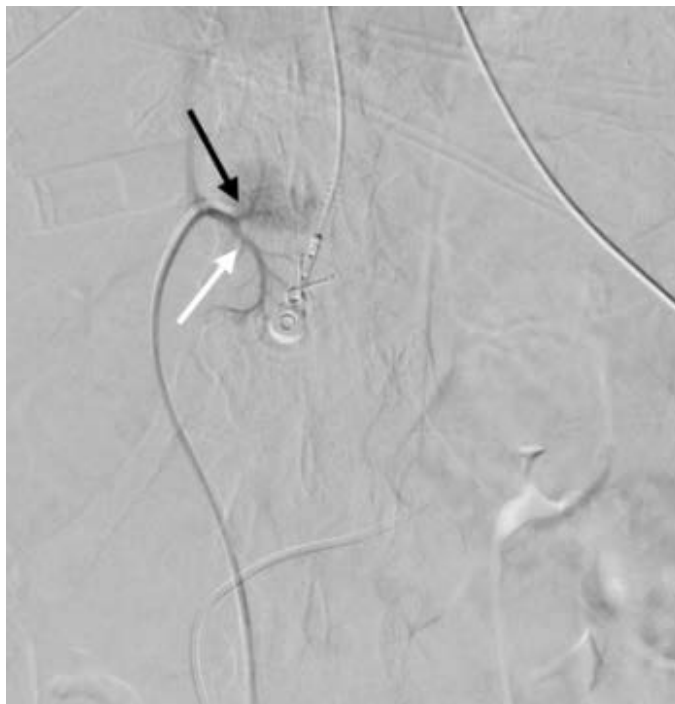
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FIGURES



**Figure 1:** Right adrenal vein inferior tributary identified on initial AVS. Notably, the vein courses medially from the IVC.



**Figure 2:** Right adrenal vein superior (black arrow) and inferior (white arrow) tributaries identified on subsequent AVS.

## KEYWORDS

*Adrenal venous sampling, primary aldosteronism, adrenal adenoma, super-selective sampling, apparent aldosterone suppression, interventional radiology.*

## ABBREVIATIONS

A/C: Aldosterone to cortisol ratio  
APA = Aldosterone Producing Adenoma  
AVS = Adrenal Venous Sampling  
CT = Computed Tomography  
IHA = Idiopathic Hyperaldosteronism  
IVC = Inferior Vena Cava  
LI = Lateralization Index  
PA = Primary Aldosteronism  
SI = Selectivity Index

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