

PERCORSO DIAGNOSTICO TERAPEUTICO DELLE LESIONI SURRENALICHE NELLA PROVINCIA DI FERRARA

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Il sampling delle vene surrenaliche – R. Galeotti

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Adrenal vein sampling (AVS) is one of the oldest procedures still performed by interventional radiologists (IRs).

The technique was first reported in the **mid-1960s** as a means to **identify the site(s) of hormone-producing adrenal** or extra-adrenal tumors causing hypertension

The procedure **gained popularity over the following two decades** but then **lost favor in the 1990s** as cross-sectional imaging techniques such as computed tomography (**CT**) and magnetic resonance (**MR**) became **widely used** and refined.



However, the **significant limitations of CT and MR** in determining the sources of excess hormone production **are now well recognized** and have caused a **resurgence of interest in AVS**.

ADRENAL VENOUS SAMPLING: THE GOLD-STANDARD FOR SURGICAL INDICATION IN PRIMARY ALDOSTERONISM

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Adrenal Vein Sampling Is the Preferred Method to Select Patients With Primary Aldosteronism for Adrenalectomy

Jaap Deinum, Aleksander Prejbisz, Jacques W.M. Lenders, Gert Jan van der Wilt Hypertension. 2018;71:10-14.

Feasibility and effectiveness of a singlecatheter approach for adrenal vein sampling in patients with primary aldosteronism BMC Endocrine Disorders (2021) 21:22

Jindong Wan^{1,2}, Fei Ran^{1,2}, Siwei Xia^{1,2}, Jixin Hou^{1,2}, Dan Wang^{1,2}, Sen Liu^{1,2}, Yi Yang^{1,2}, Peng Zhou^{1,2}

Adrenal vein sampling in the diagnosis of aldosteronism Journal of Vascular Diagnostics 2015:3 17–23

Adrenal Venous Sampling for Subtype Diagnosis of Primary Hyperaldosteronism

Mitsuhide Naruse^{1,2}, Akiyo Tanabe³, Koichi Yamamoto⁴, Hiromi Rakugi⁴, Mitsuhiro Kometani⁵, Takashi Yoneda⁵, Hiroki Kobayashi⁶, Masanori Abe⁶, Youichi Ohno⁷, Nobuya Inagaki⁷, Shoichiro Izawa⁸, Masakatsu Sone⁹

Endocrinol Metab 2021;36:965-973

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Cross sectional imaging (**CT** or magnetic resonance imaging-**MRI**) is **insensitive in detecting sub-centimeter adrenal adenomas**, which make up the **majority of APAs**. Additionally, both CT and MRI are **insensitive** to detect pathologically proven **unilateral hyperplasia**,

In patients with laboratory-confirmed PA, **cross-sectional imaging** can identify large adrenal masses concerning for malignancy, it **does not reliably distinguish unilateral from bilateral disease**, with nearly 40%–50% of patients misdiagnosed on CT or magnetic resonance imaging (MRI).

Sensitivity and specificity of **CT** and **MRI** have been reported to be 56% and 57%, and 60% and 67%, respectively. The low diagnostic yield of cross-sectional imaging is due to the **high incidence of incidental non-functioning adrenal lesions** and the presence of **microscopic nodules below the resolution** of CT or MRI.

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Adrenal vein sampling (AVS) is an uncommonly performed interventional procedure. However,it is essential in the management of patients with primary aldosteronism					

Adrenal vein sampling (AVS) is the gold standard test to localize sources of excess aldosterone

Adrenal venous sampling (AVS) is the key procedure for lateralization of primary hyperaldosteronism (PA) before surgery

Adrenal vein sampling (AVS) is **one of the oldest** procedures still performed by interventional radiologists (IRs).



The technique was first reported in the **mid-1960s** as a means to identify the site(s) of hormone-producing adrenal or extra-adrenal tumors causing hypertension



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Tecnica sequenziale

Tecnica simultanea



Feasibility and effectiveness of a singlecatheter approach for adrenal vein sampling in patients with primary aldosteronism

Jindong Wan^{1,2}, Fei Ran^{1,2}, Siwei Xia^{1,2}, Jixin Hou^{1,2}, Dan Wang^{1,2}, Sen Liu^{1,2}, Yi Yang^{1,2}, Peng Zhou^{1,2}

BMC Endocrine Disorders

(2021) 21:22

Catheterization of the **right adrenal vein** is particularly **challenging** because it is a relatively **small sized** vein with anatomical **variations**. Therefore, **localizing the right adrenal vein** during AVS **is critical for technical success**

Adrenal vein sampling: technique and protocol, a systematic review

Keith B. Quencer🝺

CVIR Endovascular (2021) 4:38

Right adrenal vein cannulation is **the most difficult part of AVS**; failure to cannulate the right adrenal vein is the most **common cause of an unsuccessful procedure**



Improving adrenal venous sampling in primary aldosteronism

Christoph Degenhart² and Martin Reincke^{*1}

Expert Rev. Endocrinol. Metab. 7(5), 531-540 (2012)

While the **catheterization** of the **left adrenal vein** can be **easily** performed in almost all cases, the catheterization of the **right adrenal vein** is substantially **more difficult** for a number of reasons

The **right adrenal vein** is very **short** and entering the IVC in **caudocranial direction**. Thus it may cause **difficulties to stabilize** the catheter in the small vein. Furthermore, there are some **other small veins** entering the IVC **nearby** the right adrenal vein, for example, **accessory hepatic veins**

Success rates for selective bilateral catheterization of the adrenal veins vary in a wide range between 31 and 98%, depending on the center and the expertise of the interventional radiologists





Corrente





















Feasibility and effectiveness of a singlecatheter approach for adrenal vein sampling in patients with primary aldosteronism

Jindong Wan^{1,2}, Fei Ran^{1,2}, Siwei Xia^{1,2}, Jixin Hou^{1,2}, Dan Wang^{1,2}, Sen Liu^{1,2}, Yi Yang^{1,2}, Peng Zhou^{1,2}

BMC Endocrine Disorders

Conclusions: The **single-catheter** approach **is feasible and effective** for AVS. Moreover, this approach required a learning curve for an inexperienced trainee

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In **sequential AVS**, the **right adrenal vein** cannulation, which is more time consuming than the left, **should be done first** thereby **decreasing the time gap** between samplings.



Adrenal venous sampling: the learning curve of a single interventionalist with 282 consecutive procedures

Diagn Interv Radiol 2018; 24:89–93

Adrenal venous sampling (AVS), the **gold standard for assessing laterality of primary aldosteronism**, is a **technically complicated** procedure with **success rates ranging between 30% and 96%.**

Satisfactory AVS success rate was achieved after approximately 36 procedures and satisfactory success rate was maintained by performing approximately 27 procedures annually.
AVS should be limited to few operators that perform sufficiently large number of procedures to achieve, and maintain, satisfactory AVS success rate

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Adrenal vein sampling **may be non-diagnostic in a significant proportion of cases**. One study that highlighted this difficulty was the German Conn registry :**Diagnostic Adequacy was achieved in only 41.1%** of procedures.

But, with proper training, knowledge and experience it can be performed successfully.

AVS is typically done at **major referral centers** and has a **greater success in the hands of interventionalists experienced** in this procedure.

The learning curve is estimated to be about 20–30 cases with maintenance of proficiency of about 15 annual cases

Adrenal Vein Sampling to Distinguish Between Unilateral and Bilateral Primary Hyperaldosteronism: To ACTH Stimulate or Not?

Tae-Yon Sung ^{1,2,*}, Wilson Mawutor Alobuia ², Monica Varun Tyagi ², Chandrayee Ghosh ² and Electron Kebebew ²

J. Clin. Med. 2020, 9, 1447;

AVS can be performed with or without adrenocorticotropic hormone (ACTH) stimulation.

Many referral centers around the world perform ACTH stimulation to avoid the problem of aldosterone and cortisol pulsatile variation and increase the gradient as compared to non-stimulation

However, there are **no specific guideline** recommendations as to whether ACTH stimulation is necessary for AVS or improves the ability to distinguish between unilateral and bilateral PA

Adrenal Venous Sampling With or Without Adrenocorticotropic Hormone Stimulation: A Meta-Analysis

Irakoze Laurent,^{1,2} Manirakiza Astère,³ Fengfan Zheng,¹ Xiangjun Chen,¹ Jun Yang,⁴ Qingfeng Cheng,¹ and Qifu Li¹

J Clin Endocrinol Metab, April 2019, 104(4):1060–1068

Catheterization is **rarely a problem with the left** adrenal vein.

When venography of the putative **right adrenal vein is atypical** or possibly represents hepatic vein, some operators will perform **C arm CT venography** to confirm the location.

However, the **most accurate** method to ensure correct sampling is **rapid cortisol analysis** of specimens before ending the procedure. Most laboratories can perform this analysis within 45–60 min.

As **cortisol** is produced **solely by the adrenal glands**, cortisol **gradient between** the **peripheral** veins and **"adrenal" vein** is used to confirm adequate adrenal vein cannulation.

There is a wide variety (\geq 1.1 to \geq 5) of **Selectivity Indices** used to determine sampling adequacy .

Selectivity Indices > 2 and > 5 are generally used as cutoffs for adequacy with unstimulated and stimulated sampling, respectively

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AVS results interpretation

Once it has been proven that both left and right AVs have been adequately sampled, the next step is to **determine if results are lateralizing to one gland**.

The aldosterone level (A) in each sample is normalized to the cortisol level (C) : $(A_{LAV}/C_{LAV} and A_{RAV}/C_{RAV})$. Then, one side is divided by the other to determine the Lateralization Index (LI):

 $LI \ge 4$ is compatible with a unilateral source of aldosterone

Adrenal vein sampling: technique and protocol, a systematic review

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Lateralization

Keith B. Quencer

Lateralization Indices (L.I.) of **> 2** for **unstimulated** and **> 4 for stimulated** sampling are recommended by the Endocrine Society

AVS is a remarkably safe procedure. Significant adverse events are very uncommon.

They include the usual **rare complications** associated with venography from the **femoral vein** (e.g., bleeding, thrombosis, contrast reaction, and contrast nephropathy).

The **specific complication** of this procedure is **injury to the** (usually **right**) **adrenal vein** from catheterization itself or more commonly over injection of contrast, leading to **vein rupture**, vein **thrombosis**, gland or **perigland hematoma**, or adrenal infarction. This complication occurs in <1% of cases in high volume centers.

Adrenal haematoma as a complication of adrenal vein sampling

Mourad Hussein Senussi,¹ Nizar Hussein Senussi,² Ahmad Alwakkaf,¹ Shawn G Kwatra¹

The patient symptomatically improved with analgesics, intravenous fluids, and did not need any surgical intervention

SIMMONS LAUGHTON

JEAN

LAURENCE

DOUGLAS OLIVIER

KIRK

However, the significant limitations of CT and MR in determining the sources of excess hormone production are now well recognized and have caused a resurgence of interest in AVS.

CHARLES

STANLEY KUBRICK FILM

SPARTACUS

PETER

USTINOV

JOHN

GAVIN

AND

TONY

CURTIS AS ANTONINE

Dekkers T, Prejbisz A, Kool LJS, et al; **SPARTACUS** Investigators.

Adrenal vein sampling versus CT scan to determine treatment in primary aldosteronism: an outcome-based randomised diagnostic trial. *Lancet Diabetes Endocrinol.* 2016 ;4:739–746

SPARTACUS trial (S ubtyping P rimary A ldosteronism: a R andomized T rial Comparing A drenal Vein Sampling and C omp u ted Tomography S can), in 192 patients with PA

We compared outcomes in patients with PA who had been managed based on either a CT scan result or an AVS result. Management consisted of adrenalectomy, if an APA was suspected, or *medical therapy* (mineralocorticoid receptor antagonist), if bilateral hyperplasia was found

After 1 year follow-up, **no significant differences** in any of the patient-important outcomes, such as **antihypertensive medication use** and **quality of life**, were observed

AVS causes **additional radiation exposure**, probably even more so when performed by less-experienced radiologists. This aspect **reduces the attractiveness** of AVS considerably but is largely **ignored by the guideline**

Our study demonstrates that the <u>AlluraClarity technology</u> upgrade enables a radiation dose reduction up to one third in patients during AVS compared to the precursor technology Allura Xper without compromising image quality.

It is true that the recent multicenter, randomized **SPARTACUS trial did not show a significant difference** in intensity of **antihypertensive drugs** given or **clinical benefit** from management based on **AVS compared with CT imaging** alone. However, **there has been substantial criticism of that study**, and most **authorities** in the field continue to **insist on AVS** prior to operation **for PA**

Response to Adrenal Vein Sampling Is the Preferred Method to Select Patients With Primary Aldosteronism for Adrenalectomy: Con Side of the Argument

Gian Paolo Rossi, John W. Funder

Hypertension. 2018;71

The evidence from the SPARTACUS trial (Subtyping Primary Aldosteronism: a Randomized Trial Comparing Adrenal Vein Sampling and Computed Tomography Scan) has been dissected at length, in the pro case and elsewhere. The authors limit their caveats to plus or minus cosyntropin, omitting key issues, such as patient inclusion (sex and age), imaging discrepancies, sequential sampling AVS recently shown to be suboptimal, unusual therapy/end points, plus statistical inadequacy— all of which disqualify the trial

To paraphrase Winston Churchill on democracy, AVS is similarly far from perfect—but until (and unless) something better comes along, it is the best we have got.

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Conclusion and future perspectives

Assuming a population of **320 million US citizens**, with more than **25%** of people affected by **hypertension** and **15%** of these cases due to **PA**, one may estimate **12 million people who may have an indication for AVS**.

As **40%** of these would be expected to be **due to aldosterone-producing adenomas** and the vast majority of patients are cured after **adrenalectomy**, we can estimate that over **4 million patients** could be **diagnosed with AVS and surgically cured**.

Close collaboration with **endocrinologists** and **surgeons** is warranted to allow **interventional radiologists** to help in treating these patients.

Università degli Studi di Ferrara

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