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PICTORIAL ESSAY

CME

Adrenal Venous Sampling for Recognising the Many Variants of Adrenal Veins: A Pictorial Essay

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INTRODUCTION

Primary aldosteronism is a leading cause of secondary hypertension. Its management lies in the determination of subtype, i.e., whether aldosterone overproduction is unilateral or bilateral. In unilateral autonomous secretion, the commonest cause is an aldosterone-producing adenoma; other causes include unilateral nodular or diffuse adrenal hyperplasia, or, rarely, carcinoma.[1] Unilateral adrenalectomy offers a definitive cure in such cases with successful normalisation of blood pressure achieved in 50% to 80% of patients and improvement in the rest.[1] In bilateral aldosterone hypersecretion, pharmacotherapy (i.e., mineralocorticoid receptor antagonists such as spironolactone) and eplerenone are the preferred treatment.

Adrenal venous sampling (AVS) is the gold standard to distinguish between unilateral and bilateral adrenal disease in primary aldosteronism. It is a challenging procedure with success rates ranging from 30% to 96%.[2] Cannulation of the right adrenal vein is the most difficult part; knowing its anatomy is key. We aimed to review the normal anatomy and variations of the right and left adrenal veins, and the techniques to achieve success based on experience in our centre.

The adrenals are highly vascularised. Arterial supply to the adrenal glands is via three adrenal arteries, namely, the superior adrenal artery arising from the inferior phrenic artery, the middle adrenal artery arising from the abdominal aorta, and the inferior adrenal artery arising from the ipsilateral renal artery.[3] They branch into several smaller arteries penetrating the adrenal capsule and supply the cortex and medulla. The adrenal veins eventually drain into the inferior vena cava (IVC), and their anatomy is described in the following section.

ANATOMY AND VENOGRAPHIC APPEARANCE OF THE ADRENAL VEINS

AVS requires accurate identification of the adrenal veins prior to catheterisation. The right adrenal vein typically drains directly into the IVC, while the left adrenal vein usually joins the inferior phrenic vein, which drains into

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the left renal vein.[4] There are typically three tributary veins to the central adrenal vein of each adrenal gland: the superior, lateral, and inferior tributary veins on the right; and the superior-median, superior-lateral, and lateral tributary veins on the left.[5] Anatomical variations of the drainage patterns have been reported in 13% of patients.[6]

Right Adrenal Vein

Failure to identify or cannulate the right adrenal vein is the most common cause of an unsuccessful procedure.[7]

The right adrenal vein is a short, straight vein which originates from the medial gland and drains directly into the IVC, usually entering posterolaterally at the T11-T12 or T12-L1 level.[8] It is shorter than the left adrenal vein, measuring 1 to 2 cm in length, and 3 to 5 mm in calibre.[8] Different venographic patterns of the right adrenal vein have been described by Daunt[7]:

1. A characteristic gland-like pattern formed by a main central vein and numerous branches (Figure 1);
2. A delta pattern with little filling of internal structures (Figure 2);

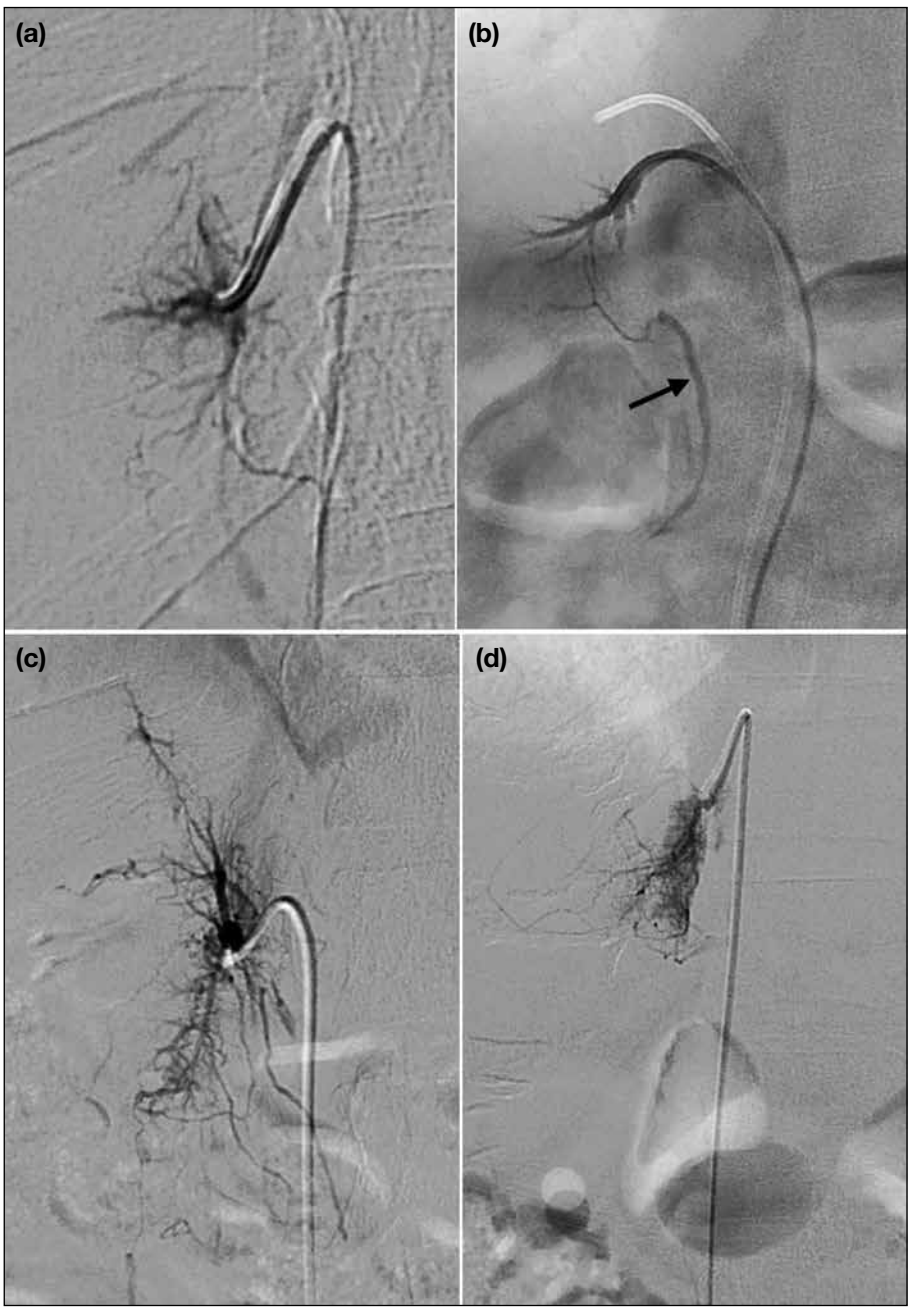

Figure 1. Digital subtraction angiogram showing gland-like pattern of the right adrenal vein. Gland-like pattern where there is typically a main central stem communicating with numerous branches. The presence of an inferior emissary vein (black arrow) confirms correct cannulation of the right adrenal vein (b).

3. A triangular pattern with crowded vessels and a blush-like appearance (Figure 3);
4. No discernible adrenal veins, but the main vessel position is characteristic and fits with the position estimated at computed tomography; and
5. Spider-like (Figure 4) or stellate (Figure 5) branches communicating with a central vein.

Communication with renal capsular, inferior phrenic, and intercostal veins is common. Cases of connection with superficial hepatic veins have also been reported.[7] Small accessory hepatic veins are common mimics of the right adrenal vein (Figure 6). Distinguishing features include: (1) communication with a larger hepatic vein; (2) the presence of hepatic parenchymal staining, which is uncommon in adrenal venography; and (3) reports of ipsilateral flank or abdominal discomfort by the patient upon contrast injection with pressure into the adrenal vein (particularly on the right side), which is typically absent in injections into hepatic veins.[7] Adrenal venous drainage into hepatic veins instead of direct drainage into the IVC is also reported (Figure 7).[8] In addition, the right adrenal vein may also take a more upward and straight course in some cases (Figure 8).

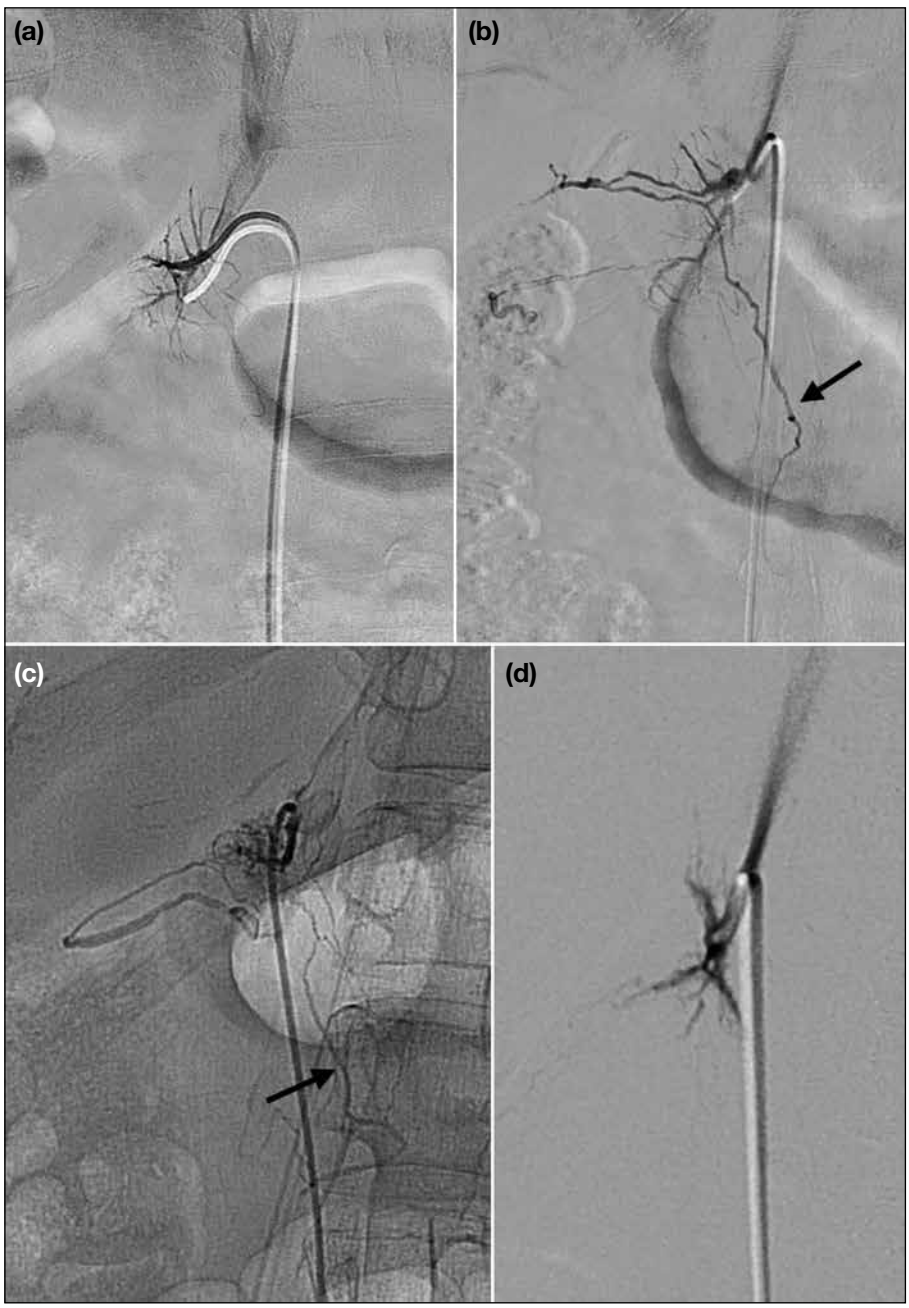

Figure 2. Digital subtraction angiogram showing delta pattern of the right adrenal vein. There may be several tributaries that converge to a short central trunk to give a delta configuration and enters the inferior vena cava directly. Glandular parenchymal stain is usually limited or negligible. Note is made of an inferior emissary vein (black arrows in [b] and [c]), the presence of which is pathognomonic for a right adrenal vein.

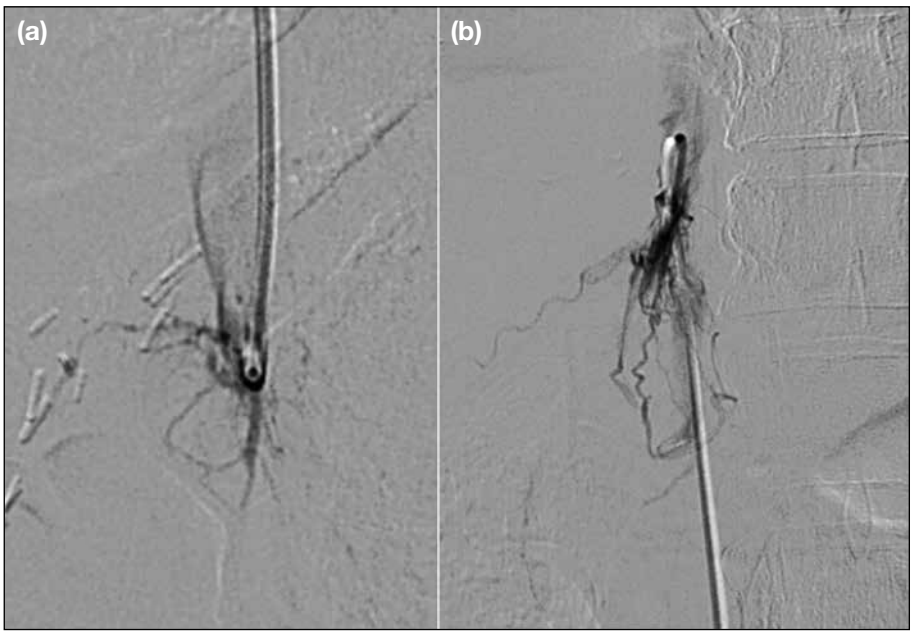

Figure 3. Digital subtraction angiogram showing triangular pattern of the right adrenal vein with relatively crowded vessels and blush-like appearance.

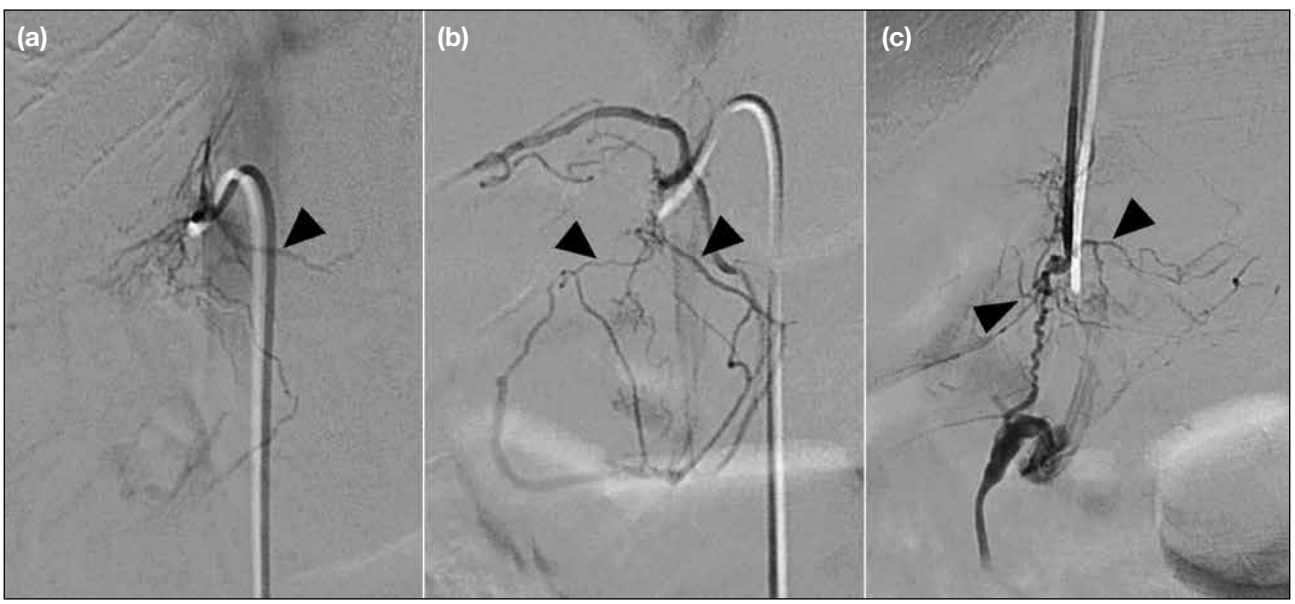

Figure 4. Digital subtraction angiogram showing the right adrenal vein. Long thin branches (black arrowheads) resembling spider legs converging to a central trunk which drains into the inferior vena cava.

With its varied venographic appearance, the only certain finding of a right adrenal vein is the presence of an inferior emissary vein, which was identified in up to 86% of successful AVS cases in a study reported by Kohi et al.[9] The Table summarises the venographic features suggesting correct cannulation of the right adrenal vein.

Left Adrenal Vein

The left adrenal vein usually joins the inferior phrenic vein to form a common phrenicoadrenal trunk, of varying length, before taking a caudal path to drain into the superior aspect of the left renal vein[8] (Figure 9). The left adrenal vein typically measures 1 to 4 cm to its confluence with the inferior phrenic vein, then approximately 1 to 3 cm from there to the left renal vein, and measures approximately 4 to 5 mm in calibre.[8] Anatomical variations include separate drainage of the left adrenal vein and inferior phrenic

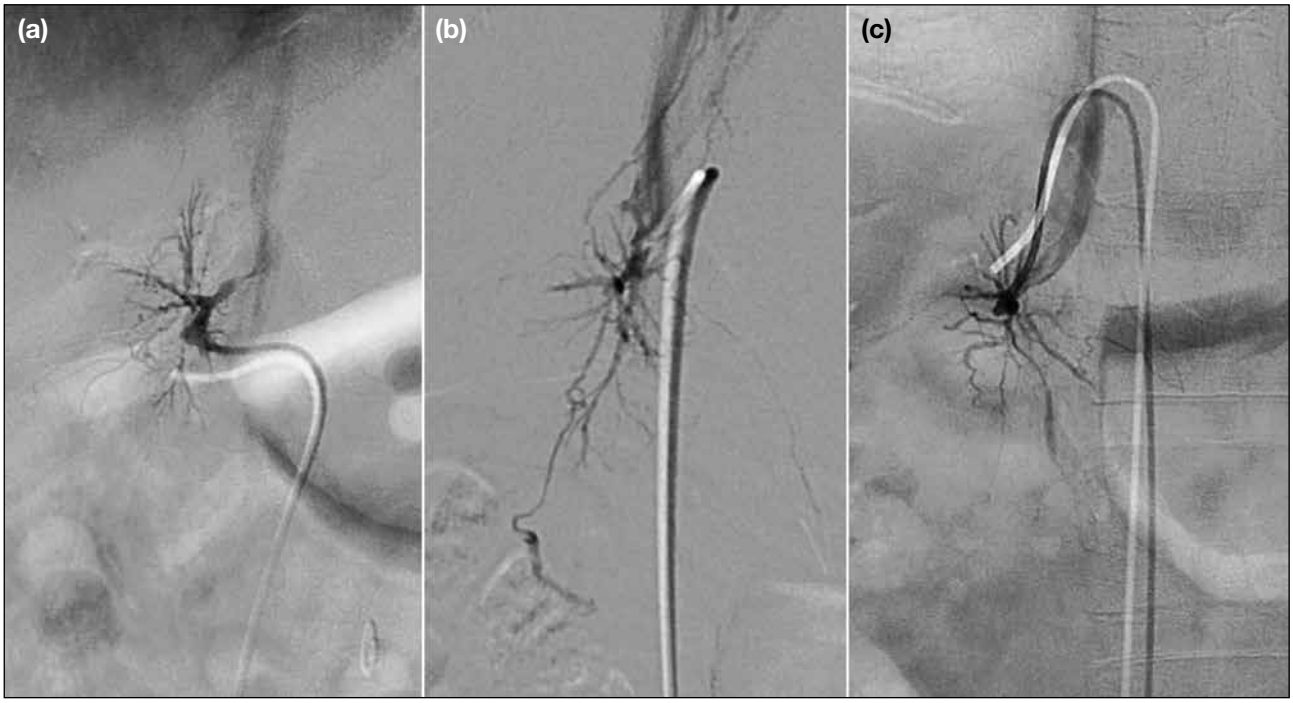

Figure 5. Digital subtraction angiogram showing stellate pattern of the right adrenal vein. Multiple short thin branches arranged in a radiating pattern like a star.

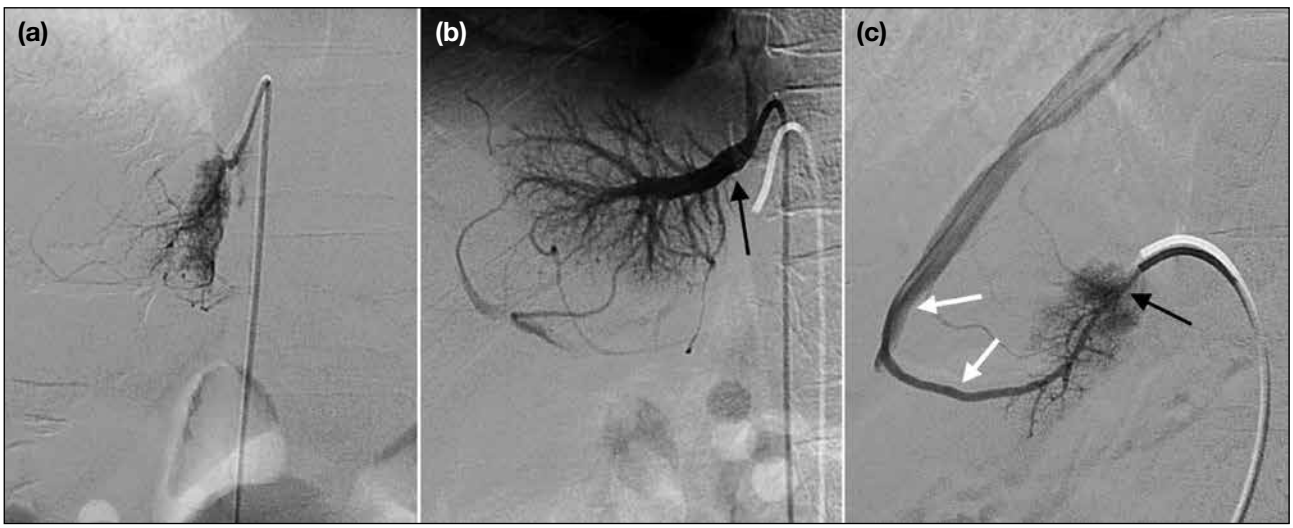

Figure 6. Digital subtraction angiogram showing the accessory hepatic vein. It is often difficult to distinguish hepatic sinusoidal staining from an accessory hepatic vein (black arrows), which is sometimes described as leaf-like pattern, as shown in (b) and (c). Absence of capsular, inferior emissary or communicating veins are consistent with hepatic vein cannulation, and intrahepatic communication to larger hepatic veins may occasionally be seen (white arrows in [c]). Another useful distinguishing feature is when the patient reports ipsilateral flank or abdominal discomfort during contrast injection into the adrenal vein with pressure (more common on the right side), which is absent in hepatic vein injections.

vein into the left renal vein. There may also be superficial, emissary, or capsular veins extending from the surface of the adrenal gland into the perirenal fat, and occasional penetration of the renal capsule. These can communicate with the inferior phrenic vein, intercostal veins, left renal vein, as well as the azygous or hemiazygos vein.[7]

There are anatomical variations of the left adrenal vein that operators should be aware of. Examples include

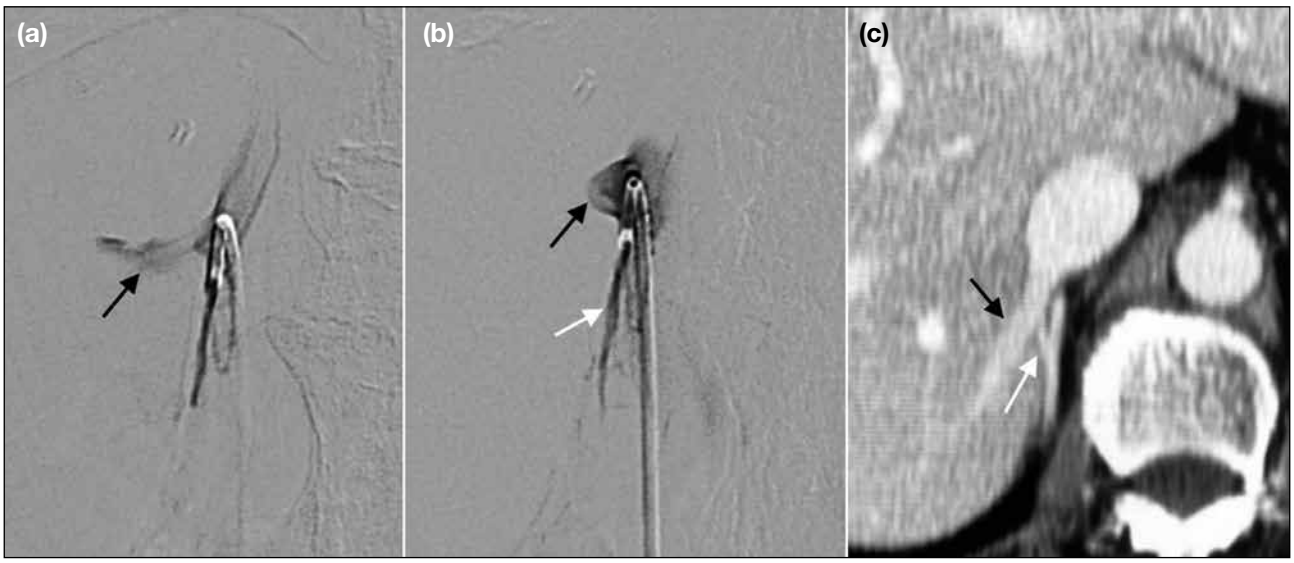

Figure 7. (a, b) Digital subtraction angiogram showing the right adrenal vein (white arrow in [b]) is seen entering a right hepatic vein (black arrows) before draining into the inferior vena cava upon adrenal venography. (c) Review of preprocedural computed tomography revealed drainage of the tiny right adrenal vein (white arrow) into a right hepatic vein (black arrow) instead of directly draining into the inferior vena cava. In this case the right hepatic vein was first cannulated with a Cobra 1 catheter, followed by cannulation of the right adrenal vein with microcatheter.

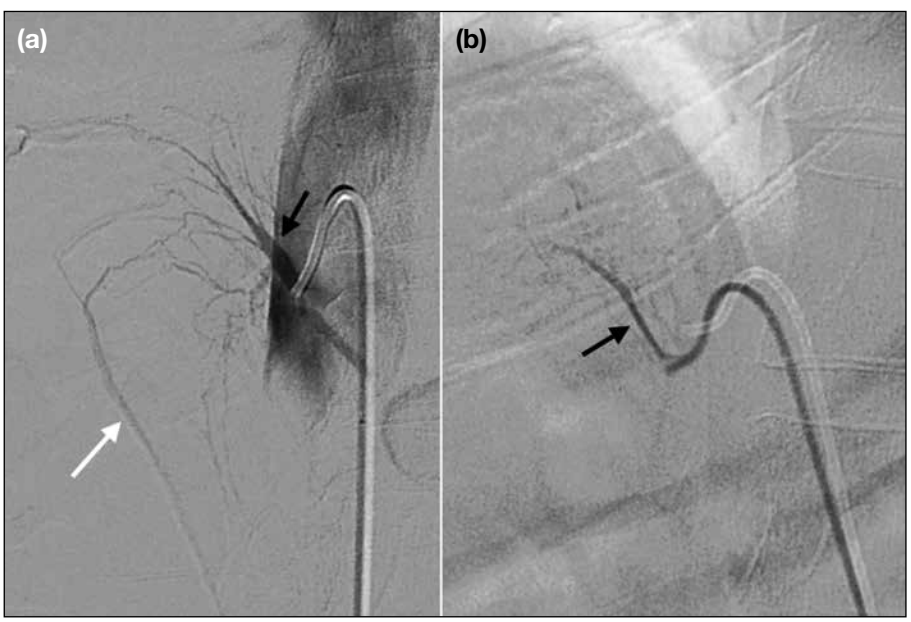

Figure 8. Digital subtraction angiogram showing the long right adrenal vein with an upward and straight course (black arrows). An inferior emissary vein is often seen (white arrow in [a]).

direct drainage of the left adrenal vein into the left renal vein without forming a common phrenicoadrenal trunk with left inferior phrenic vein, or direct drainage into the IVC[8,10] (Figure 10). There are also reported cases where the central vein may be absent or very short, with multiple adrenal tributaries draining into the phrenicoadrenal trunk directly or into the inferior phrenic vein without a central vein.[8]

PROCEDURE AND TECHNIQUE

Preprocedural computed tomography is helpful to evaluate the adrenal glands for any surgically amenable lesions which may account for the patient's clinical presentation, e.g., adrenal adenoma (Figure 11). It also allows evaluation of the anatomy of the adrenal veins and any anatomic variations, which is crucial in procedure planning.

AVS may be performed with or without pharmacological stimulation with synthetic adrenocorticotropic hormone (ACTH), known as cosyntropin. Cortisol levels may fluctuate throughout the procedure due to a number of factors, including diurnal variation, pulsatile pattern of secretion, and the effect of physiological stress, under which its concentration in the blood will surge.[2] These interfere with the indices used in the evaluation of acquired samples (see the next section). ACTH stimulation overcomes fluctuations in cortisol secretion influenced by the aforementioned factors and maximises the gradient between cortisol concentrations in the adrenal veins and that in the peripheral veins, thus increasing the confidence of successful sampling.[11] It also stimulates aldosterone secretion from aldosterone-producing adenomas that overexpress ACTH receptors, thereby increasing the chance of lateralisation.[11] A study has suggested that pharmacological stimulation with ACTH may increase blood flow to the adrenal glands, enlarging them and increasing the cannulation success rate.[11]

Table. Features suggestive of correct cannulation of right adrenal vein.

Typical venographic pattern
Relative location of the right adrenal gland with reference to the right kidney: suprarenal location
Presence of inferior emissary vein
Presence of adenoma (if applicable)
Ipsilateral flank or abdominal discomfort by the patient upon contrast injection
Important point of note: right adrenal vein never crosses the midline

Vascular access is typically acquired through puncture of the right or both common femoral veins. Access via an upper limb vein such as the basilic vein[12] has been reported (Figure 12).

The operator may opt for either sequential or simultaneous sampling methods. In sequential sampling, one adrenal vein is sampled before cannulation of the contralateral side, creating a time gap between acquisition of bilateral samples. In such cases, the right adrenal vein should be cannulated first to reduce the time gap as it is usually more time-consuming owing to its anatomy.[13] In simultaneous sampling, the catheter is placed in the first engaged adrenal vein and sampling is withheld until the contralateral side is also successfully cannulated, after which sampling is performed in a synchronous manner. Simultaneous sampling is thought to reduce the chance of creating artificial gradients between the glands due to the pulsatility of aldosterone secretion. However, this is possibly at the expense of a theoretical slight increase in risk of adrenal vein thrombosis due to lengthened duration of catheter positioning in the adrenal vein.[13] Intermittent flushing with saline may reduce the risk of

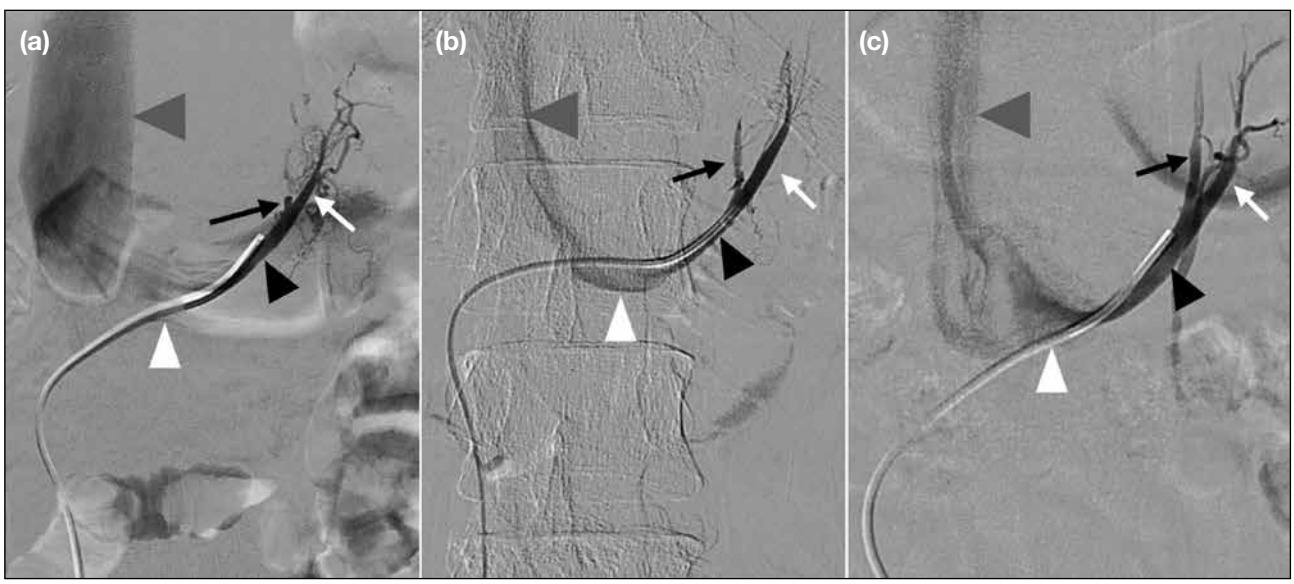

Figure 9. Digital subtraction angiogram showing normal anatomy of the left adrenal vein. The left adrenal vein (white arrows) typically joins the inferior phrenic vein (black arrows) to form a common phrenicoadrenal trunk (black arrowheads) before coursing caudally to drain into the left renal vein (white arrowheads) and subsequently the inferior vena cava (grey arrowheads).

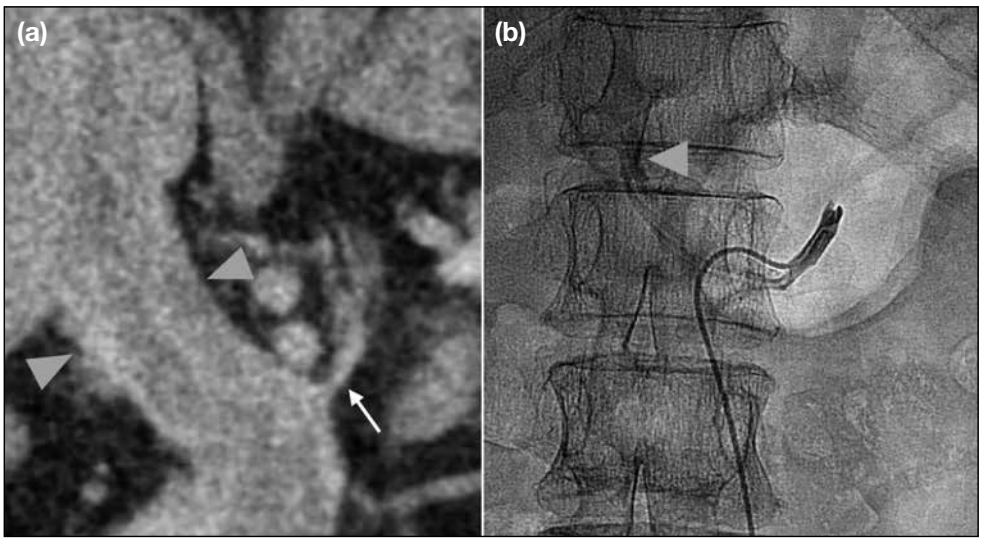

Figure 10. (a) Computed tomography and (b) digital subtraction angiogram showing anomalous left adrenal vein (white arrow in [a]) draining directly into the inferior vena cava (grey arrowheads) instead of the phrenicoadrenal trunk.[10] Sometimes an alternative catheter may be selected instead of Simmons 2, depending on the angle and curve, as well as according to the operator's preference. An SHK catheter was employed in this case as illustrated in (b).

Figure 11. (a, c) Digital subtraction angiogram showing round filling defect corresponding to adrenal adenoma. (b, d) Computed tomography (CT) showing right adrenal adenoma. Sizeable round filling defects (black arrows) are demonstrated on adrenal venography (a, c), which correspond to the adrenal adenomas (white arrows) detected on CT (b, d). These are often accompanied by the presence of multiple small tributaries.

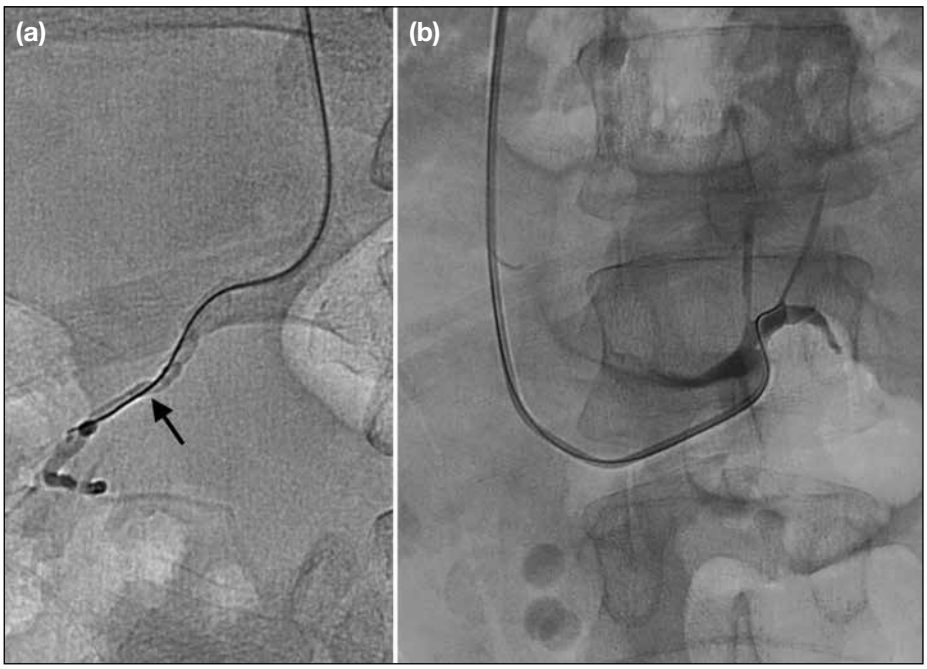

Figure 12. Digital subtraction angiogram showing transbasilic approach. Cannulation of the right adrenal vein (black arrow) with SHK catheter (a) and the left phrenicoadrenal trunk with Tiger catheter (b), with vascular access acquired via puncture of the right basilic vein. Microguidewire was used on both sides to stabilise catheter position, followed by gentle pull back of the catheters to facilitate aspiration.

adrenal vein thrombosis, though this technique should be carefully practised as it in turn poses an increased risk of catheter dislodgement from the target vein as well as sample dilution. These can be prevented by gentle injection pressure upon flushing and ensuring that initial blood samples are discarded.

Superselective AVS, also called segmental AVS, is a method whereby sampling is performed via the adrenal tributary veins in place of central adrenal veins and is thought to allow identification of aldosterone hypersecretion in specific segment(s) of the glands, thereby sparing lesion-free segments in cases where bilateral adrenalectomy is planned.[5]

Catheter selection is important to ensure effective cannulation and sampling. For the right adrenal vein, 4.1-Fr SHK catheter (Cook Medical, Bloomington [IN], US) is often the catheter of choice in our centre due to its specific curve with a soft tapered end which favours the venous anatomy in the majority of cases. The use of other catheter shapes such as Tiger[14] (Terumo Corporation, Tokyo, Japan) and specifically designed catheters such as the MK-adrenal catheter[5] (Hanaco Medical, Tokyo, Japan) have also been reported. Other options for the right side include the Simmons 1 (Cook Medical, Bloomington [IN], US), Cobra 1 and Cobra 2 (Terumo Corporation, Tokyo, Japan), and, in some cases, Mikaelsson (Boston Scientific, Marlborough [MA], US). Of particular note, catheters with large reverse curves must be used with caution, as they may result in too deep of a cannulation beyond an aldosterone-rich tributary, as well as increasing the risk of venous rupture and thrombosis.[15] The catheter is first advanced to a level from T11 to L1 and the catheter tip is rotated to face the posterior wall of the IVC. It is gently withdrawn with a slight probing motion until the catheter 'drops into' the right adrenal vein. Other veins, for example, the accessory hepatic veins, phrenic veins, or other small retroperitoneal veins, may be inadvertently cannulated throughout the search for the right adrenal vein. If no vessel is engaged, the catheter may be rotated to the right by a few degrees and advanced in the cranial direction to repeat the above manoeuvre until the right adrenal vein is engaged.[15]

For the left phrenicoadrenal trunk, with its more consistent anatomy, a Simmons 2 catheter (Cook Medical, Bloomington [IN], US) is usually selected. Once reaching the ostium of the left renal vein, the catheter is gently pulled back, causing its tip to advance further. Continued retraction will result in the catheter flicking superiorly to engage the phrenicoadrenal trunk.[7] Selective cannulation of the left adrenal vein is generally not recommended in order to avoid missing any tributaries contributing to sources of aldosterone excess, given the potential presence of the aforementioned anatomic variations.[15] One study reported paradoxically

lower aldosterone concentrations from selective central vein samples compared to phrenicoadrenal trunk samples in 17% of the cases.[16]

During AVS, owing to the small calibre of the target veins, the catheter tip commonly wedges against the venous wall, resulting in difficulty in aspiration of blood samples. Creation of side holes allows easier aspiration of blood samples when the catheter tip is wedged. In our centre, one pair of side holes is usually created by piercing the distal limb of the catheter (approximately 3 mm from the end hole) using a 21-gauge needle. We always test the integrity of the catheter before in vivo use. While the theoretical risk of catheter fracture is possible, this has not been encountered during our past 10 years of practice. In challenging cases such as small target veins or unstable cannulation, coaxial technique with microcatheters and microguidewires may be employed[17] (Figure 13).

Adrenal venograms should be performed with gentle, slow injection of a low volume of iodinated contrast to confirm correct cannulation of the target vein, and to avoid rupture of the fragile adrenal veins and resulting venous haemorrhage. Loin or back pain may be reported by the patient during contrast injection, especially into the right adrenal vein; this is absent during injection into mimics such as accessory hepatic veins.[7]

Gentle intermittent aspiration is recommended during venous sampling, as forceful suction may result in collapse of the venous wall onto the catheter tip, which hinders sampling.[15] The first 5 mL of the aspirated sample is discarded as it lowers the accuracy of serum aldosterone measurements due to contamination by iodinated contrast. Subsequently, another 10 mL is aspirated and a venogram is repeated to confirm the catheter is still within the target vein to validate the acquired sample. After sampling both the right adrenal vein and the left phrenicoadrenal trunk, 10 mL of peripheral blood is drawn from the femoral vascular sheath for biochemical confirmation of sampling success and calculations of appropriate indices for results analysis as detailed in the section below.

INDICES FOR ADRENAL VENOUS SAMPLING

The spectrum of venographic appearances of the right adrenal vein precludes reliance on venography alone to determine accurate cannulation. The most common technique to confirm the success of AVS entails measurements of hormonal concentrations in the adrenal and peripheral venous samples and calculations of the following indices.[18]

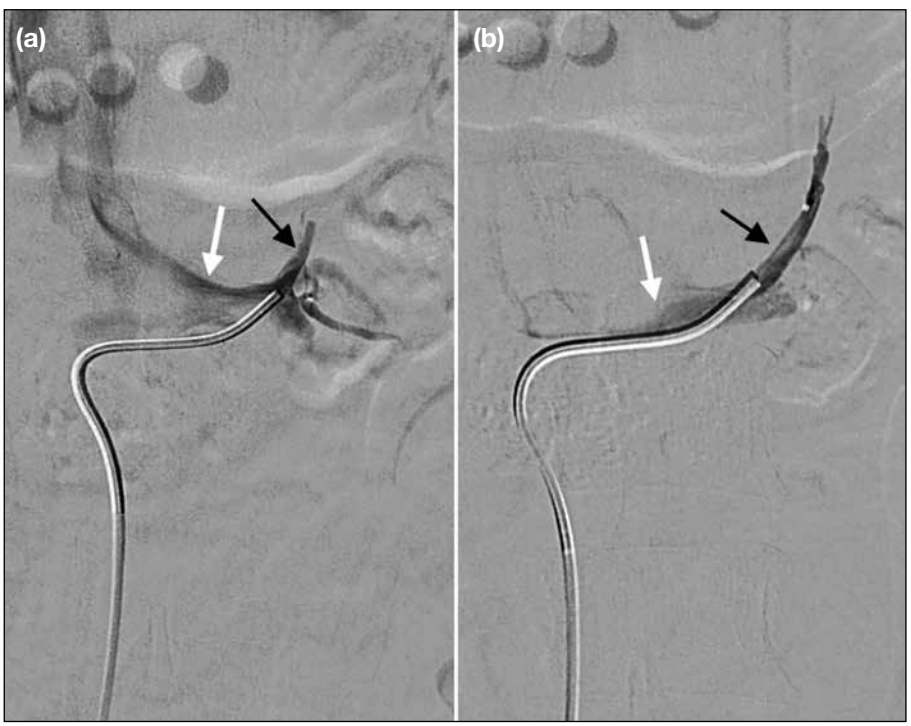

Figure 13. Digital subtraction angiogram showing cannulation of the left phrenicoadrenal trunk. The cannulation with a Simmons 2 catheter in this patient with an unstable anchor due to shallow breathing and a relatively more acute angle between the left renal vein (white arrows) and the phrenicoadrenal trunk (black arrows). Coaxial technique with the Renegade Hi-Flo (Boston Scientific, Marlborough [MA], US) microcatheter-microguidewire system was employed and sampling was successful.

The selectivity index is defined as the ratio of cortisol concentration in the adrenal veins to that in the peripheral veins. According to the Adrenal Venous Sampling International Study,[19] the majority of centres use a cutoff of 2 under non-stimulated conditions and 3 to 5 under ACTH stimulation. In our centre, where ACTH stimulation is performed, a selectivity index of 5 is taken as a cut-off for successful cannulation in accordance with the protocol established with our endocrinologists.

Lateralisation index (LI) is defined as the aldosterone-to-cortisol ratio in the dominant adrenal vein (i.e., the side with the higher aldosterone level) over the aldosterone-to- cortisol ratio in the non-dominant adrenal vein. It is used to establish whether a lateralised aldosterone excess exists. Most centres use an LI of 2 to 4 under non-stimulated conditions and 2.6 to 4 under ACTH stimulation.[19] In our centre, an LI of ≥4 suggests lateralised aldosterone excess, and an LI of <3 implies absence of lateralisation.

The contralateral suppression index is calculated by dividing the aldosterone-to-cortisol ratio in the non-dominant adrenal vein by that in the IVC. If LI is ≥3 but <4, a contralateral suppression index of <1.0 is predictive of good surgical outcome and is considered lateralised.[19]

An intraoperative rapid automated cortisol assay may also be performed to expedite confirmation of procedural success without having to render the patient at risk of a repeated invasive examination.

CONCLUSION

AVS is a technically challenging procedure with variable success rates, which is highly operator dependent. Proper recognition of normal and variant adrenal venographic findings, especially that of the right adrenal vein, is necessary for success. Variant adrenal venous anatomy influences catheter selection and sampling techniques. This pictorial review showcases different venographic patterns and anatomical variations of the adrenal gland veins in hopes of facilitating future operators to achieve safe and successful AVS.

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