

Recognizing **primary aldosteronism**: A critical, but underdiagnosed cause of worsening chronic kidney disease



New guidelines for screening and determining its underlying cause¹

Primary aldosteronism (PA) is the most common endocrine cause of hypertension. While it is rarely associated with hypokalemia, hypertension is the only defining characteristic of PA. In 2025, the Endocrine Society released an updated clinical practice guideline to encourage widespread screening for PA, increase the identification of patients with PA, and suggest treatment specific to the condition.¹

PA has broad implications for chronic kidney disease (CKD) progression. In all cases, a supraphysiologic amount of aldosterone is produced independent of renin and may enhance the risk of CKD progression. PA can also lead to a disproportionately higher risk of cardiovascular complications, including stroke, coronary artery disease, atrial fibrillation, and heart failure. These risks further increase when PA is not diagnosed and treated appropriately.

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Evolving understanding of PA

Although PA was initially defined as a rare cause of secondary hypertension, it's now understood to describe a spectrum of autonomous aldosterone secretion abnormalities and is recognized as common and underdiagnosed. At one time, PA was only suspected in individuals with both resistant hypertension and hypokalemia. Further research has found that most patients with PA do not have hypokalemia. Other studies show that PA spans a broader continuum of blood pressure control. PA has been clearly demonstrated in individuals with mild hypertension and those with normal blood pressure—populations that were not historically tested for PA.²⁻⁴

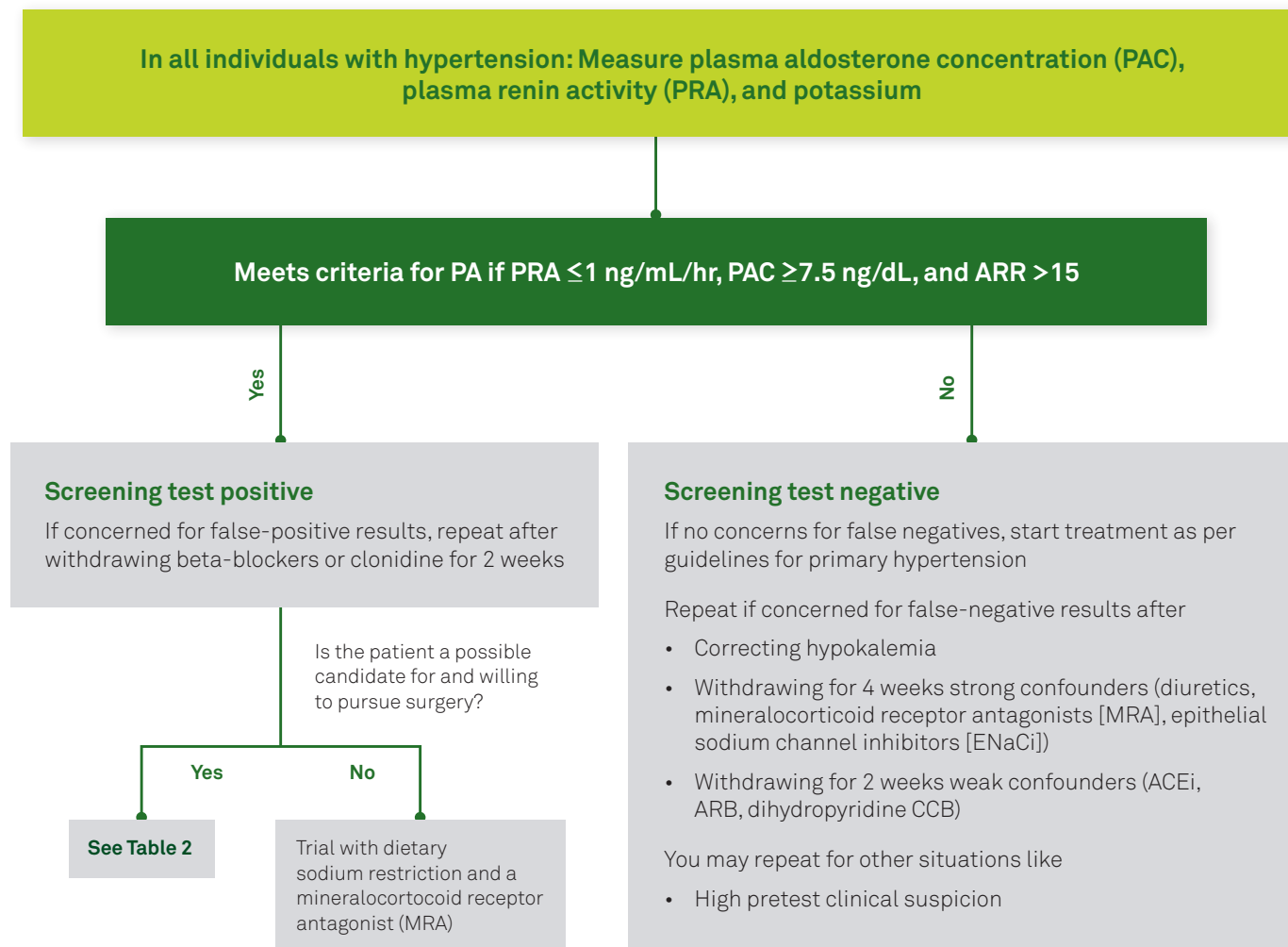
Due to this increased understanding of the prevalence of PA, suspected underdiagnosis of the condition, and effective available treatment, the 2025 guideline focuses on widespread screening, early detection of PA to reduce associated risks, and condition-specific medical/surgical treatment.¹



Table 1. Screening for primary aldosteronism

2025 Endocrine Society guidelines recommend screening all patients with hypertension for PA.

This may be done without suspending current antihypertensive medications.¹



ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARR, aldosterone-renin ratio; CCB, calcium channel blocker; CKD, chronic kidney disease; ENaCi, epithelial sodium channel inhibitor; K, potassium; MRA, mineralocorticoid receptor antagonist; PAC, plasma aldosterone concentration; PRA, plasma renin activity.

Medications with minimal interference with PAC and PRA

The following classes of medications are recommended if the physician decides to suspend the initial antihypertensive regimen when suspecting false-positive or -negative results:

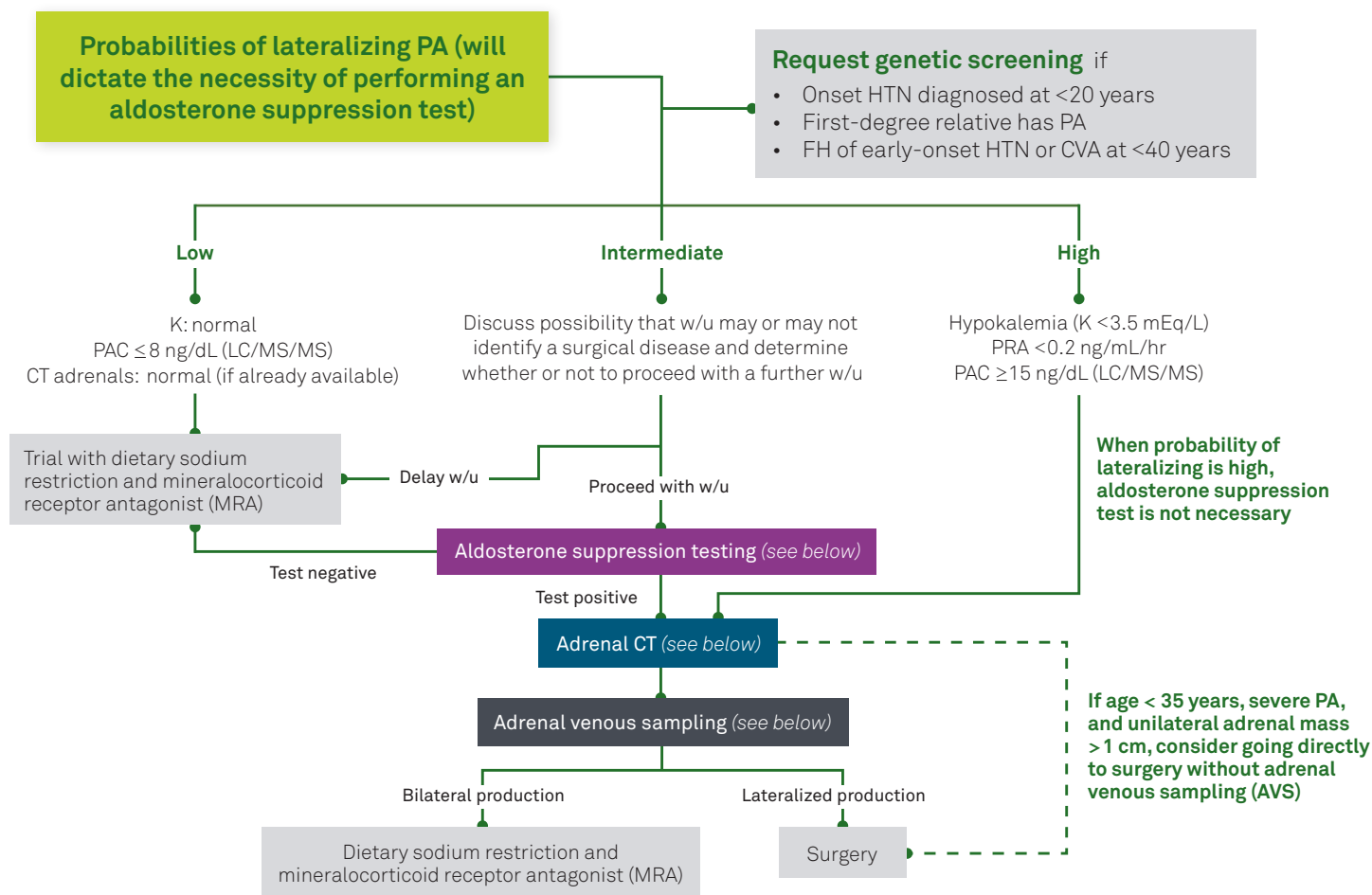
- Alpha-blockers: prazosin, doxazosin
- Nondihydropyridine CCB: verapamil
- Vasodilators: hydralazine

CKD and PA screening

In hypertensive patients with CKD, renin decreases in proportion to nephron loss, except when there is renal ischemia from renal artery stenosis, in which case, renin will be elevated. Aldosterone can also be elevated in CKD, leading to overall increases in false-positive testing.⁵

Table 2. Identifying the cause of PA¹

The patient is interested in pursuing a full workup and possibly surgery—and is a surgical candidate



Aldosterone suppression test recommended outpatient procedure: Oral Sodium Loading

Patient given 2 g NaCl tablets TID for 3 days. On day 3, start 24 hrs urine collection; send to lab requesting Na and aldosterone.

Interpretation:

If: Urine Na > 200 mEq 24 hrs, and 24 hrs urine aldosterone > 12 mg 24 hrs: the test is positive

ACTH, adrenocorticotrophic hormone; ADV, adrenal venous sampling; APA, aldosterone-producing adenoma (unilateral disease); CVA, cerebrovascular accident; D/C, discontinue; FH, family history; HTN, hypertension; HU, Hounsfield unit, a measurement of radio density used in CT images; IHA, idiopathic hyperaldosteronism (bilateral disease); IVC, inferior vena cava; K, potassium; LC/MS/MS, liquid chromatography with tandem mass spectrometry; MRA, mineralocorticoid receptor antagonist; Na, sodium; NaCl, sodium chloride; PA, primary aldosteronism; PAC, plasma aldosterone concentration; PRA, plasma renin activity; TID, 3 times daily; w/u, workup.

Adrenal CT (contrast provides more information when an adrenal nodule is present)

- Recommended to rule out **adrenocortical carcinoma**: Malignancy supported by size of lesion > 4 cm, elevated precontrast density (HU $> 10\%$) and $< 50\%$ contrast washout at 10 minutes
- Bilateral adrenal hyperplasia or idiopathic hyperaldosteronism (IHA)**: Bilateral adrenal gland thickening or micronodular changes suggest bilateral adrenal hyperplasia; however, these patients may also have normal-appearing adrenal glands on CT
- Aldosterone-producing adenoma (APA)**: A mass with density ≤ 10 HU is typically a benign adenoma. For lesion ≥ 1.5 cm, assessment for cortisol production is warranted. Microscopic APA are not visible on the CT scan. Size of APA is rarely > 1.5 cm
- PA diagnosis and presence of lateralization** of aldosterone production are based on biochemical tests, not on radiology, and **adrenal venous sampling** should be done following an adrenal CT to decide if surgery is an option: CT/MRI alone did not agree with AVS in 37% of the cases in one study

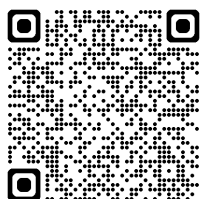
Adrenal venous sampling

- Continuous cosyntropin infusion** (50 mcg per hour started 30 minutes before sequential sampling)
- Selectivity index**: used to establish that the catheters are correctly placed in the right and left adrenal vein. The selectivity index is calculated by dividing the adrenal veins-to-IVC cortisol. The adrenal veins are successfully cannulated when the ratio is at least 5:1 when using ACTH infusion
- Lateralization index**: used to establish if aldosterone production lateralizes in APA. The lateralization index is calculated by dividing the aldosterone-to-cortisol ratio in the dominant adrenal vein by that in the nondominant adrenal vein. APA is confirmed if ratio of high side vs low side $\geq 4:1$. IHA is confirmed if ratio of high side vs low side $< 3:1$. Ratio of < 4 but > 3 are an area of overlap
- Contralateral index**: defined as the **aldosterone-to-cortisol ratio from the nondominant adrenal vein** divided by the aldosterone-to-cortisol ratio in the IVC. If the ratio is < 1 , the nondominant adrenal vein is suppressed, which is usually associated with APA

Quest Diagnostics test	Test code	CPT® code
Plasma Renin Activity (PRA) Reflex to Aldosterone, LC/MS/MS <i>If renin is suppressed, Aldosterone, LC/MS/MS (test code 17181) will be performed at an additional charge (CPT code: 82088)</i>	13817	84244
Plasma Renin Activity, LC/MS/MS	16846	84244
Aldosterone, LC/MS/MS	17181	82088
Potassium, Serum	733	84132
Aldosterone/Plasma Renin Activity Ratio, LC/MS/MS	16845	82088, 84244
Aldosterone, 24-Hour Urine (includes Creatinine)*	229	82088, 82570
Sodium, 24-Hour Urine with Creatinine	838	84300, 82570
Aldosterone/Cortisol Ratio, Adrenal Vein Sampling, 1 Site	19573	82088, 82533

* Creatinine, 24-Hour Urine may be ordered separately with test code 381.

For more information, visit
QuestDiagnostics.com/PrimaryAldosteronism



Scan the QR Code to listen to the
“Rethinking Primary Aldosteronism diagnosis”
episode of our Healthier World podcast

References

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- Mehdi A, Rao P, Thomas G. Our evolving understanding of primary aldosteronism. *Clev Clin J Med.* 2021;88(4):221-227. doi: 10.3949/ccjm.88a.20166
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- Wang Q, Dong H, Li H, Zuo Y, Zou Y, Jiang X. Aldosterone-to-renin ratio changes in patients with renal artery stenosis and aldosteronism. *J Clin Hypertens.* 2025;27(3):e70031. doi: 10.1111/jch.70031

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