

PRIMARY ALDOSTERONISM (PA) SCREENING - KEY POINTS:



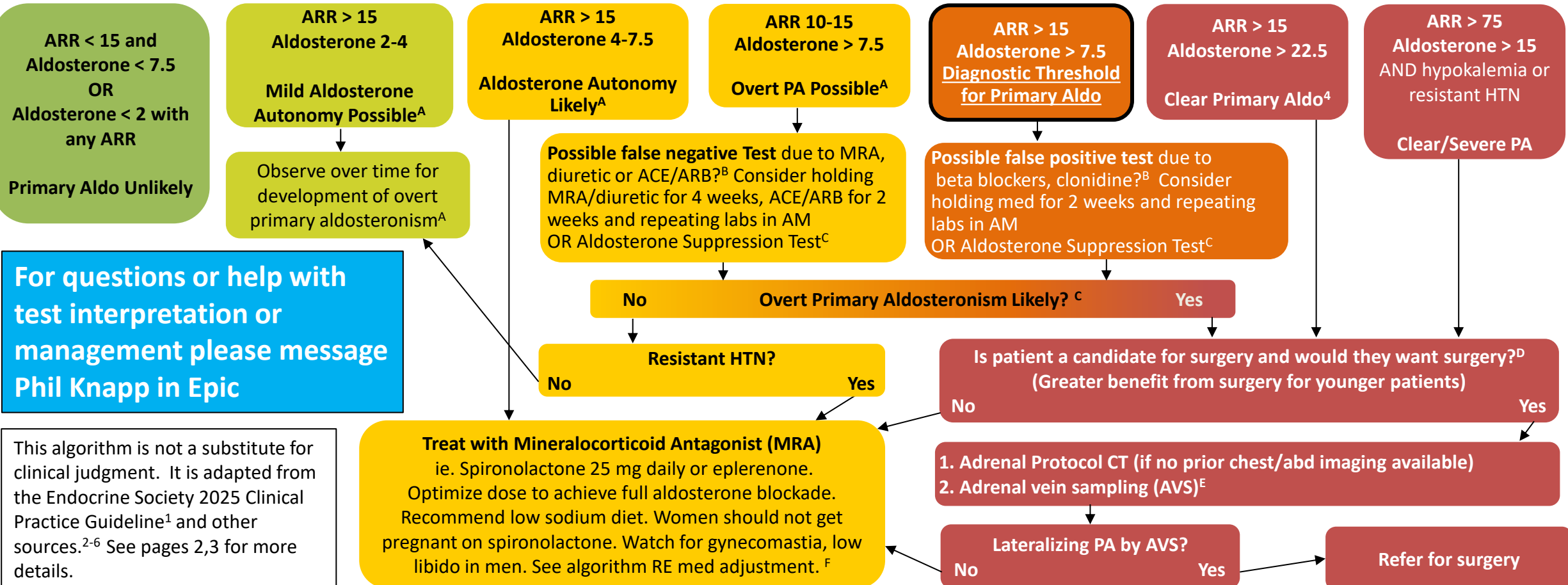
- Primary aldosteronism is present in 5-10% of all patients with hypertension and approximately 20% of patients with resistant HTN¹
- Primary aldosteronism is an independent risk factor for cardiovascular events and development / progression of CKD²
- Endocrine Society guidelines from 2025 recommend screening all patients with HTN for primary aldosteronism¹
- AHA / ACC guideline from 2025 recommend screening all patients with resistant HTN or HTN with other risk factors (hypokalemia, OSA, DM?)³

Patients seen in BMC Endocrine Clinic for diabetes care who have hypertension should be screened for primary aldosteronism as follows:

- **Check simultaneous aldosterone, plasma renin activity (PRA), K⁺ and calculate the aldosterone / renin ratio (ARR)**
- Meds do not need to be changed before testing. If K⁺ is low replete and repeat labs (AM is better when possible)

Algorithm assumes aldosterone measured by LC/MS-MS as used in the BMC laboratory

Severity of primary aldosteronism / Likelihood of lateralizing disease / Benefit from evaluation for surgery
Low -----> High



Primary Aldosteronism Evaluation Details

A. Mild aldosterone autonomy and overt primary aldosteronism (PA) are a spectrum⁵ and may progress with time. There is clear evidence for targeted treatment of overt PA but patients with mild aldosterone autonomy and hypertension may also benefit from treatment with an MRA especially those with resistant HTN. Worsening of hypertension or development of hypokalemia should prompt retesting for PA in patients with previously borderline test results. Alternatively, patients with suspected mild PA can simply be started on treatment with an MRA. Patients with mild PA are less likely to have lateralizing PA and so it is appropriate to start medical therapy without evaluation for possible surgery.

B. Aldo / renin levels can be checked while on any medications, at any time of day but the results should be interpreted with an understanding of the potential effects of meds and other factors. Hypokalemia should be corrected prior to testing. If needed, medications can be temporarily held or changed and the tests repeated for potential false negative (FN) of false positive (FP) ARR. These are the most important potential effects:

Medication / Factor	Aldosterone	Renin	ARR	Washout Period
Hypokalemia	↓↓	-	↓↓ (FN)	-
PM vs. AM blood draw	↓	-	↓ (FN)	-
MRA	↑	↑↑	↓↓ (FN)	4 weeks
Diuretics	↑	↑↑	↓ (FN)	4 weeks
ACE-I / ARB	↓	↑	↓ (FN)	2 weeks
Beta blockers, clonidine	-	↓	↑ (FP)	2 weeks

Alternative medications that do not interfere with the testing include verapamil, alpha blockers and hydralazine.

References:

1. Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline. JCEM, Volume 110, Issue 9, September 2025. <https://doi.org/10.1210/clinem/dgaf284>
2. Monticone et al. *Lancet Diabetes Endocrinol* E Pub November 9, 2017
3. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults. *Hypertension* 82:10
4. Umakoshi et al. JCEM 105: 1284–1289, 2020
5. Brown et al. *Ann Intern Med*. 2020;173:10-20
6. Hundemer et al. *Lancet Diabetes Endocrinol*. E Pub 11/2017

C. Aldosterone suppression testing (AST) eg. the saline infusion test or salt-suppressed 24-urine aldosterone was previously utilized as “confirmatory” testing for primary aldosteronism but is no longer recommended routinely for that purpose since these tests do not provide better diagnostic accuracy than the ARR. They can still be used to confirm an equivocal diagnosis in certain situations, but the 2025 Endocrine Society now frames them primarily as a way to assess the severity of PA and therefore the likelihood of lateralizing disease since the two are closely correlated. For that reason, AST can help select patients who should further be evaluated for imaging and adrenal vein sampling (AVS), particularly in settings where access to AVS is limited. This not the case at BMC.

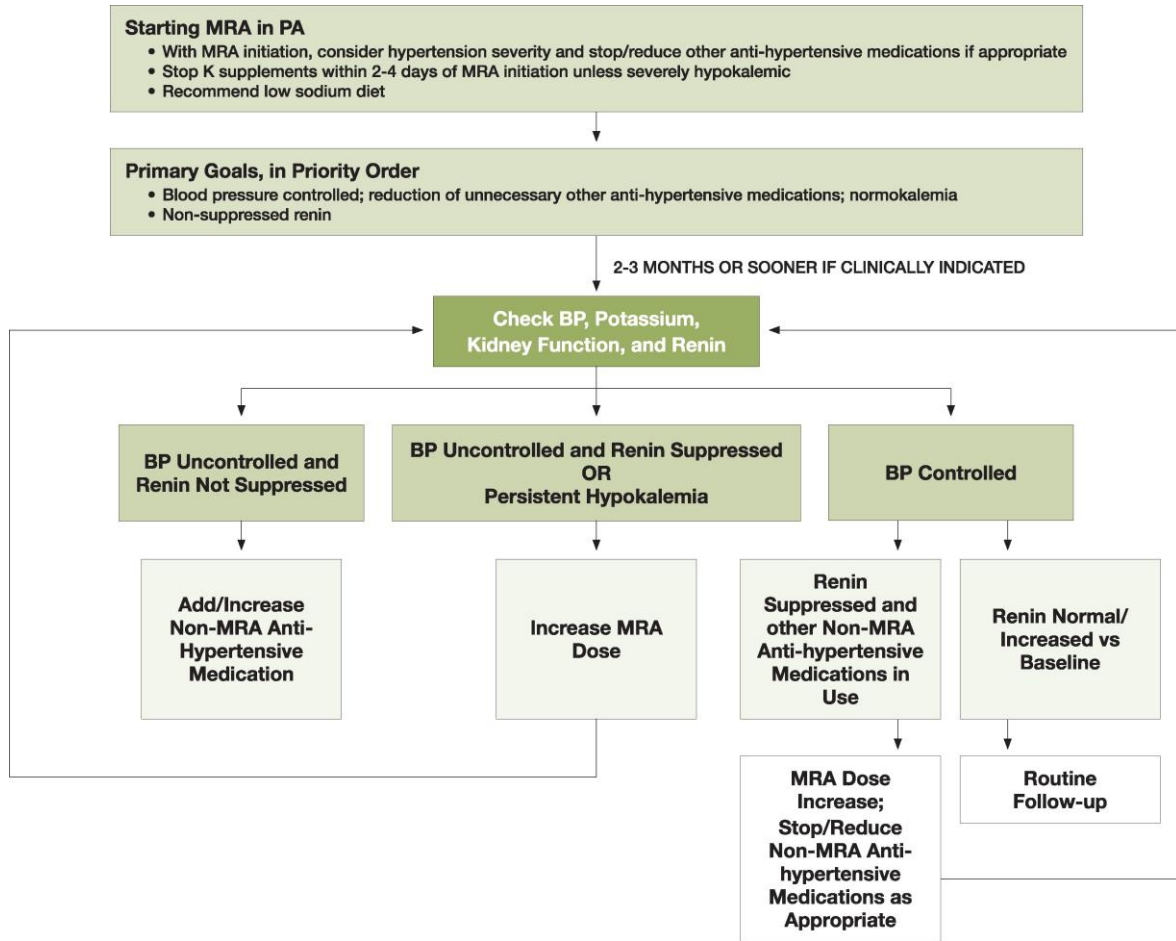
D. The decision to pursue evaluation for possible surgery for PA depends on multiple factors including patient age, co-morbidities and patient preference. There is evidence that for patients with lateralizing PA, surgery appears to be more effective than medical therapy at reducing the risk of CV events however treatment with adequate dosing of an MRA appears to achieve similar benefits.⁶ Successful surgery will eliminate the need for potassium supplementation and likely reduce the number of antihypertensives required. Laparoscopic adrenalectomy is well tolerated with a fairly quick recovery and relatively low risk. Medical therapy requires ongoing monitoring.

E. Adrenal vein sampling (AVS) is done in Interventional Radiology and ordered in Epic as “IR Venous Sampling”. Pre-procedure labs should be ordered including CBC, INR, PTT, creat and K⁺. Potassium should be repleted to the mid normal range prior to the procedure. AVS can be done in patients still on a MRA as long as the renin remains suppressed. Patients receive moderate sedation during AVS and need to be accompanied to return home.

F. See next page for instructions on initiating and adjusting therapy with a mineralocorticoid receptor antagonist (MRA).

Initiating and following MRA therapy

(Adapted from Endocrine Society 2025 guideline)



There is a wide range of inter-patient responsiveness to varying doses of MRA. The process of MRA initiation and titration is expected to be multi-step for many patients; each MRA adjustment is followed by an assessment of both BP and biochemical response, then re-entering the treatment algorithm as appropriate. The primary goal of therapy is control of BP. The secondary goal of therapy is achievement of normokalemia. Measurement of renin (as a marker of MR blockade) may assist in the process of MRA dose titration for achieving these goals and possibly reducing other non-MRA antihypertensive drugs.

1. Clinicians may **start at a relatively low dose MRA** (spironolactone 12.5-25 mg/d or eplerenone 25 mg daily or twice daily). Medically complex or frail individuals and those in whom MRA–drug interactions (eg, with an ACE inhibitor or ARB) are possible may need careful monitoring. For individuals with more severe PA, especially if profound hypokalemia is present, a higher initial dose could be considered (spironolactone 50 mg/d or eplerenone 50 mg twice daily).
2. All individuals should get **routine monitoring** of serum electrolytes, renal function, and renin within 2 to 3 months of starting MRA therapy; more frequent serial measurements may be needed in those with prior severe hypokalemia or renal impairment.
3. **Salt restriction** with a target of <85.5 mmol/d sodium is recommended (representing <5 g/d salt intake). Dietary salt restriction is a critical part of determining response to MRA therapy; individuals should be explicitly instructed on and assisted with dietary salt reduction strategies. An ongoing high-salt diet is a very common reason for apparent nonresponse to MRA therapy.
4. **MRA dose changes** to target BP control should occur at 8- to 12-week intervals, and the full drug effect may take up to 3 months in more severe PA forms. Typical doses required to de-suppress renin are variable and likely higher than doses used as empiric add-on for resistant hypertension; most individuals will achieve renin de-suppression with spironolactone doses between 50 and 100 mg/day (or eplerenone 50 to 100 mg BID). Spironolactone may be increased in 25- to 50-mg increments, and eplerenone in 25- to 100-mg increments. With each MRA dose change, repeat electrolytes, renal function, and renin 2 to 3 months later is recommended. When possible, consider off-titration of other anti-hypertensives. Once renin is de-suppressed, and if further BP reduction is required, other non-MRA antihypertensives should be added or uptitrated. If blood pressure is controlled on MRA monotherapy, there is insufficient evidence to suggest further MRA dose increases in response to low renin levels alone.
5. Normalization of **serum potassium** usually occurs, even with lower-dose MRAs, in the first 3 to 5 days, so it is reasonable to reduce or discontinue any potassium supplements at day 2 to 4 of MRA initiation in all but the most severe hypokalemic cases. Individuals who do require ongoing potassium supplementation require frequent careful monitoring of potassium.
6. The **glomerular filtration rate (GFR)** may decrease in individuals with PA on introduction of PA-targeted medical therapy or with successive titration of MRA. The time course of change may be over days to weeks and, in most cases, represents a marker of treatment efficacy as opposed to adverse effect. The natural history of an appropriate treatment-induced decrease in GFR is usually one of eventual long-term stability, anticipating a renal-sparing effect of effective MRA therapy. If renal function progressively declines, consider referring to nephrology and discontinuing ACE inhibitors or ARBs.
7. **Gynecomastia from spironolactone** is dose-related and may appear as early as 1 to 2 months into therapy but more commonly after ≥6 months of treatment. Eplerenone does not cause gynecomastia and is a good alternative in men who develop it on spironolactone.
8. **Routine follow-up** after MRA dose optimization should generally consist of blood pressure monitoring, along with annual measures of potassium and kidney function. Patients with chronic kidney disease or other risk factors for impaired renal function/electrolyte disorders (eg, combination MRA and ACE inhibitor/ARB drugs) should undergo biochemical monitoring more frequently. Routine repeat renin measures are not necessary unless re-entering the MRA titration algorithm due to incomplete BP/potassium control.