

Aldosterone-Renin Ratio

Introduction

The following information for aldosterone-renin ratio (ARR) testing is provided to ensure proper preparation for specimen collection and test interpretation

- Table 1 provides a list of medications that have minimal effects on aldosterone levels
- Table 2 lists factors that may lead to false-positive or false-negative ARR results

See ARUP Consult for [Aldosteronism](#) topic (arupconsult.com/content/aldosteronism)

Suggested Approach to Measuring ARR

(Funder, Endocrine Society Guideline, 2016)

Preparation

- Attempt to correct hypokalemia
 - Measure plasma potassium in blood collected slowly with syringe and needle (preferably not Vacutainer to minimize risk of spuriously raising potassium)
 - Avoid fist clenching – wait at least 5 seconds after tourniquet release to insert needle
 - Separate plasma from cells within 30 minutes of collection
 - Plasma K⁺ of 4 mmol/L – aim of supplementation
- Encourage patient to liberalize (rather than restrict) sodium intake
- Withdraw agents that markedly affect ARR for at least 4 weeks prior to testing
 - Spironolactone, eplerenone, amiloride, triamterene
 - Potassium-wasting diuretics
 - Products derived from licorice root (eg, licorice, chewing tobacco)
- If ARR testing is not diagnostic after withdrawing above agents and hypertension can be controlled with noninterfering medications, test again in 2 weeks after withdrawing other medications
 - Beta blockers, methyldopa, clonidine, calcium channel blockers, ACE inhibitors, angiotensin receptor blockers

- If necessary to maintain hypertension control, begin use of other antihypertensive medications that have lesser effects on the ARR
 - See Table 1
- Oral contraceptives and hormone replacement therapy may lower direct-renin concentration (DRC) and cause false-positive ARR when DRC, rather than plasma-renin activity (PRA), is measured
 - Do not withdraw oral contraceptives unless confident of alternative-effect contraception

Conditions for blood collection

- Collect midmorning after patient has been sitting, standing, or walking for at least 2 hours, and seated for 5-15 minutes
- Collect blood carefully and avoid stasis and hemolysis during collection
- Maintain sample at room temperature (not on ice) during transport to laboratory and centrifugation
 - Rapid freeze the plasma component pending assay

Factors when interpreting results

- Age
 - >65 years of age – renin can be lowered more than aldosterone by age alone, leading to raised ARR
- Gender
 - Premenstrual, ovulating females have higher ARR levels than age-matched men, especially during luteal phase of menstrual cycle when false positive can occur, but only if renin is measured as DRC and not PRA
- Time of day, recent diet, posture, length of time in posture
- Medications
- Method of blood collection
- Level of potassium
- Level of creatinine – renal failure can lead to false-positive ARR

ARR test results

- Positive or equivocal – requires confirmation
- Negative – primary aldosteronism (PA) unlikely
- Factors that may lead to false-positive or false-negative ARR results (Funder, Endocrine Society Guideline, 2016)
 - See Table 2

Tests to Consider

Primary tests

[Aldosterone/Renin Activity Ratio 0070073](#)

- Screen and diagnose hyperaldosteronism

[Aldosterone and Renin, Direct with Ratio 2002582](#)

- Screen and diagnose hyperaldosteronism

[Aldosterone, Urine 0070480](#)

- Screen and diagnose hyperaldosteronism

[Aldosterone, Serum 0070015](#)

- The combined aldosterone/renin tests are preferred when screening for hyperaldosteronism
 - Refer to Aldosterone/Renin Activity Ratio (0070073) or Aldosterone and Renin, Direct with Ratio (2002582)

[Aldosterone 60 Minutes 0070017](#)

- Use in aldosterone stimulation testing

[Aldosterone 30 Minute 0070016](#)

- Use in aldosterone stimulation testing

Related tests

[Renin Activity 0070105](#)

- The combined aldosterone/renin tests are preferred when screening for hyperaldosteronism
 - Refer to Aldosterone/Renin Activity Ratio (0070073) or Aldosterone and Renin, Direct with Ratio (2002582)

[Renin, Direct 2001575](#)

- The combined aldosterone/renin tests are preferred when screening for hyperaldosteronism
 - Refer to Aldosterone/Renin Activity Ratio (0070073) or Aldosterone and Renin, Direct with Ratio (2002582)

References

Funder JW, Carey RM, Mantero F, Murad H, Reincke M, Shibata H, Stowasser M, Young WF. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2016; 101(5): 1889-916

Table 1. Medications with Minimal Effects on Plasma Aldosterone Levels that Can Control Hypertension During Case Finding and Confirmatory Testing for PA*

	Verapamil (slow release)	Hydralazine	Prazosin hydrochloride	Doxazosin mesylate	Terazosin hydrochloride
Class	Non-dihydropyridine slow-release antagonist calcium channel	Vasodilator	α-adrenergic blocker	α -adrenergic blocker	α -adrenergic blocker
Usual dose	90-120 mg	10-12.5 mg [†]	0.5-1 mg [†]	1-2 mg [†]	1-2 mg [†]
Frequency	2x daily	2x daily	2-3x daily	1x daily	1x daily
Comments	Use singly or in combination with other agents listed in table	Commence slow-release verapamil first to prevent reflex tachycardia Commencement at low doses reduces risk of side effects‡	Monitor for postural hypotension		

*Adapted from The Endocrine Society (Funder, 2016)
[†]Increasing as required
[‡]Side effects include headaches, flushing, and palpitations

Table 2. Factors that may Lead to False-positive or False-negative ARR Results*

Factor	Effect on aldosterone plasma levels	Effect on renin levels	Effect on ARR
Medications†			
ACE inhibitors	↓	↑ ↑	↓ (false negative)
Angiotensin II type 1 receptor blockers			
Potassium-sparing diuretics	↑	↑ ↑	↓ (false negative)
Ca ²⁺ blockers (dihydropyridine)	→ ↓	↑	
Potassium-wasting diuretics	→ ↑	↑ ↑	
Central alpha-2 agonists (eg, clonidine, α-methyldopa)	↓	↓ ↓	↑ (false positive)
Nonsteroidal anti-inflammatory drugs			
β-Adrenergic blockers	↓	↓ ↓	
Renin inhibitors	↓	↓ ↑	↑ (false positive); ↓ (false negative)
Potassium status			
Hypokalemia	↓	→ ↑	↓ (false negative)
Potassium loading	↑	→ ↓	↑
Dietary sodium			
Sodium loaded	↓	↓ ↓	↑ (false positive)
Sodium restricted	↑	↑ ↑	↑ (false negative)
Age			
>65	↓	↓ ↓	↑ (false positive)
Premenopausal females‡			
Compared with males	→ ↑	↓	↑ (false positive)
Other conditions			
Malignant hypertension	↑	↑ ↑	↓ (false negative)
Pregnancy			
Renovascular hypertension			
Pseudohypoaldosteronism type 2	→	↓	↑ (false positive)
Renal impairment			

*Adapted from the Endocrine Society; Funder, 2016

†Renin inhibitors lower PRA but raise DRC. This would be expected to result in false-positive ARR levels for renin measured as PRA and false negatives for renin measured as DRC.

‡In premenopausal, ovulating women, plasma aldosterone levels measured during the menses or the proliferative phase of the menstrual cycle are similar to those of men but rise briskly in the luteal phase. Because renin levels are lower, the ARR is higher than in men for all phases of the cycle, but especially during the luteal phase during which aldosterone rises to a greater extent than renin. False positives can occur during the luteal phase, but only if renin is measured as DRC and not PRA. In preliminary studies, some investigations have found false positives on the current cutoffs for women in the luteal phase. Accordingly, it would seem sensible to screen women at the follicular phase, if practicable.