Aldosterone-Renin Ratio

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Primary aldosteronism occurs when aldosterone production is inappropriately high in relation to the patient's sodium status which causes cardiovascular damage, hypertension, and retention. Aldosterone-renin ratio (ARR) is the most reliable method for screening for primary aldosteronism. ARR is determined by measuring both aldosterone and renin concentrations. Renin concentrations may be determined by measuring direct renin concentrations or renin activity. ARR testing requires specific procedures to properly prepare for specimen collection. Additionally, a variety of factors must be accounted for when interpreting results.

For more information about the diagnosis and management of aldosteronism, refer to the Endocrine Society guideline.[1]

Featured ARUP Testing

Aldosterone/Renin Activity Ratio 0070073

Method: Quantitative Chemiluminescent Immunoassay (CLIA)/Quantitative Enzyme-Linked Immunosorbent Assay (ELISA)

- Initial test for primary aldosteronism
- Test includes direct measurement of aldosterone and measurement of renin activity
- Aldosterone-renin ratio is determined by calculation

Aldosterone and Renin Direct, With Ratio 3005949

Method: Qualitative Chemiluminescent Immunoassay (CLIA)

- Initial test for primary aldosteronism
- Test includes direct measurement of aldosterone and renin
- Aldosterone-renin ratio is determined by calculation

Testing Protocol

Patient Preparation

- Make attempt to correct hypokalemia; when measuring plasma potassium make sure to[1]:
  - Collect blood using syringe and needle
  - Avoid fist clenching during collection
  - Wait ≥5 seconds after tourniquet release to achieve needle insertion
  - Ensure that plasma separates from cells within 30 minutes of collection
- Encourage patient to not drestrict sodium intake[1]
- Withdraw interfering agents[1]:
  - At least 4 weeks before collection, withdraw agents that may have a significant effect on ARR:
    - Triamterene, amiloride, eplerenone, and spironolactone
    - Potassium-wasting diuretics
    - Any products developed from licorice root (eg, chewing tobacco, licorice)
  - If results are inconclusive after withdrawing above agents, withdraw agents with a less significant effect on ARR at least 2 weeks before collection:
    - Nonsteroidal anti-inflammatory drugs, central α-2 agonists, β-adrenergic blockers
    - Renin inhibitors, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and dihydropyridine calcium channel antagonists
  - If necessary to control hypertension prior to ARR measurement, begin use of another antihypertensive medication with lesser effects on ARR:
    - Verapamil slow release (a nondihydropyridine slow-release antagonist calcium channel)
    - Hydralazine (a vasodilator)
    - Prazosin hydrochloride (an α-adrenergic blocker)
    - Doxazosin mesylate (an α-adrenergic blocker)
    - Terazosin hydrochloride (an α-adrenergic blocker)
- Establish whether patient is taking oral contraceptives or receiving hormone replacement therapy because estrogen can result in a false-positive when using direct renin measurement for ARR.[1]
  - Withdrawal of oral contraceptives is not required; aldosterone-renin activity ratio should be considered when oral contraceptives or hormone replacement therapy are in use.

Conditions for Blood Collection

- If measuring renin activity, collect midmorning after patient has been out of bed ≥2 hours and after patient has been seated 5-15 minutes.[1]
- If measuring direct renin, collect midmorning (7-10 a.m.) after patient has been out of bed ≥30 minutes; if taking an upright sample, patient should be seated for 5-15 minutes; if taking a supine sample, patient should be in the supine position for ≥30 minutes.[1]
- Collect blood carefully and avoid stasis and hemolysis during collection.[1]
- Maintain sample at room temperature (not on ice) during both transport to laboratory and before centrifugation and rapid freezing of the plasma component pending assay.[1]

Test Interpretation

Interpretive Factors to Consider

Factors Affecting ARR Results				
Factor	**Effect on Plasma Aldosterone Concentrations**	**Effect on Renin Concentrations**	**Effect on ARR**	**Potential False Result**
Medications				
ACE inhibitors	↓	↑↑	↓	False negative
Angiotensin II type 1 receptor blockers	↓	↑↑	↓	False negative
β-adrenergic blockers	↓	↓↓	↑	False positive
Ca2+ blockers (dihydropyridine)	↔ or ↓	↑	↓	False negative
Central alpha-2 agonists (eg, clonidine, α-methyldopa)	↓	↓↓	↑	False positive
Nonsteroidal anti-inflammatory drugs	↓	↓↓	↑	False positive
Potassium-sparing diuretics	↑	↑↑	↓	False negative
Potassium-wasting diuretics	↔ or ↓	↑↑	↓	False negative
Renin inhibitors	↓	↓ (PRA) ↑ (DRC)	↑ (PRA) ↓ (DRC)	False positive (PRA) False negative (DRC)
Electrolyte Status				
Hypokalemia	↓	↔ or ↑	↓	False negative
Potassium loaded	↑	↔ or ↓	↑	—
Sodium loaded	↓	↓↓	↑	False positive
Sodium restricted	↑	↑↑	↑	False negative
Demographics				
Age >65 years	↓	↓↓	↑	False positive

[a]In premenopausal, ovulating women, plasma aldosterone concentration is similar to that of men (and renin concentrations are lower) in all phases except the luteal phase. ARR is generally higher in women than in men, and it increases even further during the luteal phase.

[b]If possible, screening during the follicular phase may reduce the likelihood of false positives. When screening during the luteal phase, renin should be measured as PRA (rather than DRC) to avoid false positives.

↔, normal; ↑, increased; ↓, decreased; ↑↑, more significant increase; ↓↓, more significant decrease; ACE, angiotensin-converting enzyme; DRC, direct renin concentration; PRA, plasma renin activity

Source: Funder, 2016[1]

Factor	Effect on Plasma Aldosterone Concentrations	Effect on Renin Concentrations	Effect on ARR	Potential False Result
Premenopausal, ovulating individuals[a]	↔ or ↑	↓	↑	False positive[b]
Other Conditions				
Malignant hypertension	↑	↑↑	↓	False negative
Pregnancy	↑	↑↑	↓	False negative
Pseudohypoaldosteronism type 2	↔	↓	↑	False positive
Renal impairment	↔	↓	↑	False positive
Renovascular hypertension	↑	↑↑	↓	False negative

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Source: Funder, 2016[1]

Results

Result	ARR	ARR	Clinical Interpretation[a]
	Aldosterone/Renin Activity Ratio 0070073	Aldosterone and Renin Direct, With Ratio 3005949	
Positive	>25[b]	>3.7	Suggestive of hyperaldosteronism; requires confirmation
Negative	≤25	≤3.7	Primary aldosteronism unlikely

[a]See Factors Affecting ARR Results table.

[b]If aldosterone concentration is >15 ng/dL.

Limitations

- Reference intervals for serum aldosterone are based on normal sodium intake.
- Aldosterone and Renin Direct, With Ratio (3005949) should not be used for patients being treated with cathepsin B.
- Aldosterone/Renin Activity Ratio (0070073) is preferred for menstruating females and those taking medications containing estrogen.

References

1. Funder JW, Carey RM, Mantero F, et al. The management of primary aldosteronism: case detection, diagnosis, and treatment: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2016;101(5):1889-1916.

Related Information

Primary Aldosteronism
Primary Aldosteronism Testing Algorithm