Aldosterone-Renin Ratio

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 levels. Renin levels 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 taken into account for proper test interpretation.

For more information about the diagnosis and management of aldosteronism, see the Endocrine Society Guidelines.[1]

Tests to Consider

Aldosterone/Renin Activity Ratio 0070073

Method: Quantitative Chemiluminescent Immunoassay/Quantitative Enzyme-Linked Immunosorbent Assay

- Use to screen and diagnose aldosteronism
- Test includes direct measurement of aldosterone and measure of renin activity; aldosterone-renin ratio is determined by calculation

Aldosterone and Renin, Direct with Ratio 2002582

Method: Quantitative Chemiluminescent Immunoassay

- Use to screen and diagnose aldosteronism
- Test includes direct measurement of aldosterone and renin; aldosterone-renin ratio is determined by calculation

For more aldosterone and renin tests, see Related Tests

Testing Protocol

Patient Preparation

- Make attempt to correct hypokalemia; when measuring plasma potassium make sure to:
  - 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 liberalize and not restrict sodium intake
- Withdraw interfering agents
  - 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 hypertension must be controlled, consider treating with slow-release verapamil, hydralazine, prazosin hydrochloride, doxazosin mesylate, and terazosin hydrochloride
- 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

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.
- 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 Aldosterone Plasma Levels	Effect on Renin Levels	Effect on ARR	Potential False Result

Factor	Effect on Aldosterone Plasma Levels	Effect on Renin Levels	Effect on ARR	Potential False Result
Medications[a]				
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
Premenopausal adult cisgender females[b]	↔ or ↑	↓	↑	False positive[b]
Other Conditions				
Malignant hypertension	↑	↑↑	↓	False negative
Pregnancy	↑	↑↑	↓	False negative
Pseudohypoaldosteronism type 2	↔	↓	↑	False positive
Renal impairment	↔	↓	↑	False positive

[a]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.

[b]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.

↔, normal; ↑, increased; ↓, decreased; ↑↑, more significant increase; ↓↓, more significant decrease; DRC, direct renin concentration; PAC, plasma aldosterone concentration

Source: Funder, 2016[1]

Factor	Effect on Aldosterone Plasma Levels	Effect on Renin Levels	Effect on ARR	Potential False Result
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 2002582	
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 (2002582) 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

Aldosteronism
Hyperaldosteronism Testing Algorithm

Related Tests

Aldosterone 30 Minute 0070016

Method: Quantitative Chemiluminescent Immunoassay

Aldosterone 60 Minute 0070017

Method: Quantitative Chemiluminescent Immunoassay

Aldosterone Inferior Vena Cava 3000484

Method: Quantitative Chemiluminescent Immunoassay

Aldosterone Right Adrenal Vein 3000486

Method: Quantitative Chemiluminescent Immunoassay

Aldosterone, Serum 0070015

Method: Quantitative Chemiluminescent Immunoassay

Aldosterone, Urine 0070480

Method: Quantitative Chemiluminescent Immunoassay

Renin Activity 0070105

Method: Quantitative Enzyme-Linked Immunosorbent Assay

Renin, Direct 2001575

Method: Quantitative Chemiluminescent Immunoassay

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