

Don't Forget about the Other A in the RAAS; Primary Aldosteronism Is More Common Than You Think

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Visual Abstract by Sophia L. Ambruso

Recent data demonstrate that primary aldosteronism is much more common than previously believed (1). Despite common perceptions among many providers, most patients with primary aldosteronism do not have hypokalemia (2, 3). Importantly, patients with treatment-resistant hypertension have a particularly high prevalence of primary aldosteronism (~20%) (1, 4). Primary aldosteronism is associated with increased risk of development and progression of chronic kidney disease, heart disease, and mortality (5). Nonetheless, primary aldosteronism responds to treatment with a mineralocorticoid receptor antagonist and is curable with adrenalectomy in some patients (i.e., those with an aldosterone-secreting adrenal adenoma or who lateralize on adrenal vein sampling) (6).

Accordingly, clinical guidelines (7, 8) recommend testing for primary aldosteronism in patients with treatment-resistant hypertension. However, recent studies from local health systems suggest that <3% of individuals who meet guideline criteria are screened for primary aldosteronism (9–11). Similarly, clinical experience suggests that many overt cases of primary aldosteronism—with all the classical features and resulting cardiometabolic complications—go undiagnosed and without proper treatment for years (6).

In a national cohort of 269,010 veterans with new-onset, apparent treatment-resistant hypertension (i.e., elevated blood pressure on at least three antihypertensive agents or controlled blood pressure requiring at least four antihypertensive agents) from 2000 to 2017, we found that just 1.6% of veterans underwent testing for primary aldosteronism (with concomitant measurement of plasma aldosterone and renin on or after meeting criteria for resistant hypertension) (12) (Visual Abstract). Patients whose initial visit was with a nephrologist or an endocrinologist were about twice as likely to undergo testing as those seen by a primary care provider or cardiologist. Testing for primary aldosteronism, regardless of the results of testing, was associated with a fourfold higher likelihood of receiving a mineralocorticoid receptor antagonist compared with no testing. This observation argues against the possibility that clinicians usually bypass testing and simply prescribe a mineralocorticoid receptor antagonist for patients with resistant hypertension. In addition, we observed that blood pressure was better controlled over time in patients who underwent testing.

Our work is consistent with prior studies demonstrating low rates of testing for primary aldosteronism in smaller, local health systems (9). Together, the studies show a lack of appropriate testing for primary aldosteronism, which is currently neglected relative to its impact on patients.

Overall, we observed ample missed opportunities for appropriate testing and treatment of patients with resistant hypertension. Our findings suggests that there are critical gaps in provider knowledge of the im-

portance of screening patients with resistant hypertension for primary aldosteronism and that there are likely barriers to implementing appropriate antihypertensive management in these patients. ■

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Conflicts of interest: Dr. Byrd holds an NIH grant investigating novel approaches to diagnosing excess mineralocorticoid receptor activation and is an inventor on a provisional patent for a novel diagnostic test related to primary aldosteronism. He has served on an advisory board for Phase Bio, which is developing an aldosterone synthase inhibitor. Dr. Cohen holds NIH grants investigating optimization of antihypertensive management in high-risk patient populations.

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What are the Testing Rates for Primary Aldosteronism and Evidence-based Hypertension Management in Treatment-resistant Hypertension Among Veterans?



Cohort

Retrospective EHR review
Veterans N = 269,010
2000-2017

Resistant hypertension
- 2x BP checks of $\geq 140/90$ mmHg x1 month
&
- 3 BP drugs including a diuretic OR
- 4 BP drug classes

Measurements

Rate of primary aldosterone testing (plasma aldosterone-renin)
Testing associated with MRA treatment and longitudinal systolic BP (SBP)

Findings

1.6% patients tested for primary aldosteronism were identified

Higher likelihood of testing if index visit was with nephrologist or endocrinologist*

HR 2.05 (1.66-2.52)

HR 2.48 (1.69-3.63)

*compared to primary care

Testing associated with

MRA use in treatment
HR 4.10 (3.68-4.55)

Lower SBP over time
-1.47mmHg (-1.64 to -1.29mmHg)

Conclusion Among veterans with apparent treatment-resistant hypertension, testing for primary aldosteronism was rare and was associated with higher rates of evidence-based treatment with MRAs and better longitudinal BP control.

Cohen JD et al. Testing for primary aldosteronism and mineralocorticoid receptor antagonist use among U.S. veterans. *Ann Intern Med*, 2020. https://doi.org/10.7326/M20-4873

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