



AVS vs CT to guide treatment choice in primary aldosteronism: An outcome-based randomized diagnostic trial

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Introduction

Primary aldosteronism (PA), the most common cause of secondary hypertension, has a prevalence of 5-10% in the general hypertensive population, which increases to 20% among patients with treatment-resistant hypertension. PA is caused, in over 90% of cases, by bilateral adrenal hyperplasia or by an aldosterone-secreting adenoma. Less commonly, PA may be due to unilateral hyperplasia, adrenal cancer or a genetic disorder. The guidelines of the Endocrine Society published in 2016 (1) have expanded the number of patients to screen for PA (table).

Hypertensive Patients To Screen for PA	
Hypertension's characteristics	Sustained: >150/100 in 3 measurements in different days. Resistant: BP above goals despite 3 different anti-hypertensives.
Hypertension associated with	Hypokalemia. Adrenal Incidentaloma. Sleep Apnoea.
Family History	Juvenile onset hypertension and/or stroke. PA in first-degree relatives.

The guidelines recommend that all patients undergo contrast-enhanced CT to rule out adrenal carcinoma (1). Sensitivity of the CT in detecting adenomas <10 mm is however suboptimal, and the CT does not establish whether the adenoma is secreting. If the patient is a candidate for surgery, the guidelines also recommend preoperative adrenal venous sampling (AVS), performed by an experienced radiologist, in order to differentiate unilateral vs. bilateral forms of PA. According to the guidelines, there may be no need for pre-surgical AVS if a hypertensive patient younger than 35 years presents with spontaneous hypokalemia, high serum concentration of aldosterone and a unilateral lesion attributable to adenoma at the CT (1). Systematic reviews suggest that failure to perform AVS following CT may lead to an inappropriate adrenalectomy in 15% of cases while erroneously exclude from surgery 19% of patients (2). AVS, however, is invasive, expensive, not completely standardized and requires a radiologist with experience in the procedure. The authors of the article discussed here (3) have examined patients with PA randomly assigned to AVS- or CT-based treatment, and compared the outcomes.

Methods

The study is a multicenter controlled trial of 200 patients with PA, enrolled between 2010 and 2013. After randomization to CT or AVS, the patients underwent adrenalectomy (if unilateral adenoma) or treatment with mineralocorticoid receptor antagonists (spironolactone or eplerenone) if bilateral hyperplasia.

Inclusion criteria: age >18 years, hypertension treated with ≥ 3 drugs at adequate dosage, or hypertension associated with spontaneous or drug-induced hypokalemia. PA confirmed with oral sodium loading test or intravenous saline infusion test.

Exclusion criteria: pregnancy, possible adrenal carcinoma, severe comorbidities, interfering treatment, suspected *glucocorticoid-remediable* PA.

Following randomization, control and intervention groups were balanced in regard to: age, sex, blood pressure (BP) readings, number of anti-hypertensive medications and hypokalemia (present in 68% of the patients in both groups).

AVS was carried out during infusion of ACTH, based on the following criteria:

- Selection Index ≥ 3 (an index of proper cannulation of adrenal veins);
- Lateralization index ≥ 4 (an index of the ability to differentiate uni- vs. bilateral PA based on the lateralization of aldosterone release);
- Contralateral Suppression Index ≤ 1 .

Patients undergoing AVS had received preliminary CT for evaluation of the anatomy of adrenal vessels.

Follow-up at 1 year (184 patients):

- 92 patients treated on the basis of the CT (46 undergoing adrenalectomy, 46 on pharmacologic treatment);
- 92 patients treated on the basis of the AVS (46 undergoing adrenalectomy, 46 on pharmacologic treatment).

Primary endpoint: intensity of anti-hypertensive treatment required at 1-year follow-up to reach target BP, defined as BP $< 135/85$ on 24h BP recording.

Secondary endpoints: Quality of life (QoL, evaluated with questionnaire RAND-36); cost/effectiveness ratio; biochemical outcomes in patients undergoing adrenalectomy and who underwent repeated oral sodium loading test or intravenous saline infusion test; adverse events.

Results

There have been no significant differences between patients treated on the basis of CT or AVS in relation to the primary endpoint, nor in relation to QoL or adverse events:

- Target BP reached in 42% of the patients treated on the basis of CT results vs. 45% in patients treated on the basis of AVS results ($p = 0.82$);
- Among the patients undergoing adrenalectomy, biochemical normalization achieved in 80% of the patients treated on the basis of CT results vs. 89% in patients treated on the basis of AVS results ($p = 0.25$).

A non-significant advantage in quality-adjusted life-years (QALYs) was found in the AVS group, associated with a significant increase in mean health-care costs. A 50% discordance rate was observed in the AVS group when the results of the AVS were confronted with the TC results.

Discussion

The current study shows that at 1-year follow-up there are no significant differences in BP control whether the patient underwent preliminary CT or AVS. According to the authors, neither of the two tests can be considered as a gold standard in the identification of an aldosterone-secreting adenoma. These results do not support current guidelines which recommend a CT in all patients with PA, followed by pre-operative AVS if the patient is a candidate for surgery (with the exception discussed above) (1).

References

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3. Dekkers T, Prejbisz A, Kool LJ, et al. Adrenal vein sampling versus CT scan to determine treatment in primary aldosteronism: an outcome-based randomised diagnostic trial. *Lancet Diabetes Endocrinol* [2016, 4: 739-46](#).