Adrenal Venous Sampling With or Without Adrenocorticotropic Hormone Stimulation: A Meta-Analysis

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Context: Adrenal venous sampling (AVS), with or without adrenocorticotropic hormone (ACTH) stimulation, is the test of choice to identify patients with a surgically curable subtype of primary aldosteronism (PA). Whether AVS with ACTH stimulation is more effective than AVS without ACTH stimulation remains controversial.

Objective: To compare the effectiveness of AVS with ACTH stimulation and AVS without ACTH stimulation in patients with PA.

Design: The Cochrane Library, PubMed, Embase, and Web of Science databases were searched to identify relevant articles. All cohort studies comparing the two techniques (AVS with ACTH stimulation and AVS without ACTH stimulation in a patient with PA) were included in the analysis.

Results: A total of 14 studies met the inclusion criteria, and they were analyzed. AVS with ACTH stimulation did not significantly reduce the number of incorrect lateralization more than AVS without ACTH stimulation in patients with PA (OR: 0.76; 95% CI: 0.36, 1.59; $P = 0.47$). AVS with ACTH stimulation significantly reduced the number of unsuccessful cannulations of both adrenal veins more than AVS without ACTH stimulation in patients with PA (OR: 0.26; 95% CI: 0.17, 0.40; $P < 0.00001$). For subgroup analyses, it also significantly reduced the number of unsuccessful cannulations of left adrenal vein and right adrenal vein (OR: 0.14, 95% CI: 0.06, 0.33, $P < 0.00001$; and OR: 0.30, 95% CI: 0.12, 0.71, $P = 0.007$, respectively).

Conclusion: AVS with ACTH stimulation can significantly reduce the number of unsuccessful cannulations, without significantly reducing the number of incorrect lateralization. Further studies are still needed to verify these findings. ***(J Clin Endocrinol Metab* 104: 1060–1068, 2019)**

Primary aldosteronism (PA) is the most common form of endocrine hypertension (1). It is characterized by an autonomous aldosterone production causing sodium retention, plasma renin suppression, hypertension, cardiovascular damage, and increased potassium excretion, leading to variable degrees of hypokalemia (2). It is now well known that patients with PA have an increased risk of cardiovascular and cerebrovascular events and target organ damage (heart and kidney) relative to patients with essential hypertension and a matched cardiovascular-risk profile or compared with the general population with hypertension (1, 3).

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Abbreviations: ACTH, adrenocorticotropic hormone; AVS, adrenal venous sampling; LI, lateralization index; PA, primary aldosteronism; SI, selectivity index.

The diagnosis of PA requires three steps, including screening, confirmation, and subtype differentiation (4). The last step is fundamental, because some subtypes, such as aldosterone-producing adenoma and unilateral adrenal hyperplasia, can benefit from adrenalectomy, whereas others, such as bilateral adrenal hyperplasia should be treated pharmacologically with mineralocorticoid receptor antagonists (4, 5).

Adrenal venous sampling (AVS) is the test of choice to identify patients with a surgically curable subtype of PA (6). The success of AVS is determined by the correct cannulation of the adrenal veins (2, 7). It is measured by the selectivity index (SI), which is calculated as the ratio of cortisol in the adrenal vein and in a peripheral vein. The cannulation of the adrenal veins is particularly challenging on the right side. The right adrenal vein is small and has a complicated anatomy, and there is a high risk of displacement of the cannula as a result of respiratory motion (8).

Lateralization index (LI; aldosterone-to-cortisol ratio in the ipsilateral adrenal vein divided by aldosterone-to-cortisol ratio in the contralateral adrenal vein) is used to differentiate a unilateral from a bilateral source of aldosterone excess (9, 10). However, the LI is sometimes considered together with a requirement for contralateral suppression of aldosterone production to define lateralization (2, 11).

An AVS procedure with an exogenously administered synthetic derivative of adrenocorticotropic hormone (ACTH 1-24; called cosyntropin) is used in some centers to minimize stress-induced fluctuations in aldosterone secretion in no simultaneous AVS, to maximize the gradient in cortisol from the adrenal vein to the inferior vena cava, and to maximize aldosterone secretion from an aldosterone-producing adenoma (12). However, some concerns have been raised on the possible stimulation of aldosterone production from the contralateral adrenal gland (nondominant gland) in unilateral PA (2). Nonetheless, cosyntropin use has been shown to improve the technical success rate of AVS (13).

It is important to note that different cutoff values of SI and LI are used in different centers during the AVS procedure. Most centers use an SI cutoff of at least two to three under basal conditions and three to five under ACTH stimulation, with a minority of the centers using more permissive SI criteria under a basal condition ($\geq$1.1 or 1.36) (14). There is not a wide consensus on the optimal cutoff for LI (14). A recent study has demonstrated the use of more stringent criteria for LI ($\geq$4) after ACTH stimulation (15).

Nevertheless, the 2016 Endocrine Society Guideline considered SI $\geq$ 2 without ACTH stimulation and SI $\geq$ 5 with ACTH stimulation as benchmarks for correct adrenal vein cannulation (16). It also considered LI $\geq$ 2 without ACTH stimulation and LI $\geq$ 4 with ACTH stimulation as the preferred thresholds for lateralization.

Many studies have been recently conducted and compared the outcomes between AVS with ACTH stimulation and AVS without ACTH stimulation in patients with PA (4, 17, 18). However, the controversies about the usefulness of ACTH stimulation during AVS procedure remain unresolved (10, 19, 20).

To analyze further the effectiveness of ACTH stimulation during the AVS procedure, we performed a meta-analysis and compared AVS with ACTH with AVS without ACTH.

Materials and Methods

Study selection and data extraction

The PubMed, EMBASE, Web of Science, and Cochrane library databases were searched for relevant papers. The last search was performed on 14 May 14 2018. To identify all of the relevant studies, the search terms were "adrenal venous sampling" (or "AVS"), "adrenocorticotropic hormone" ("ACTH"), "lateralization," and "primary aldosteronism."

The eligibility criteria were as follows: the study (i) where AVS with ACTH stimulation is compared with AVS without ACTH stimulation in patients with PA; (ii) should be written in English; (iii) should be published as full text; (iv) should be with complete outcomes, such as pathology outcome, surgery outcome, or clinical outcome; (v) should contain data on incorrect lateralization (wrong or missed lateralization) and/or unsuccessful cannulation in adrenal veins that could be extracted. The studies that did not fulfill the eligibility criteria were excluded.

To assess specifically the effects of ACTH stimulation during AVS procedure, the included studies were divided into the following four subgroups: (i) comparison between AVS with ACTH stimulation and AVS without ACTH stimulation based on incorrect lateralization; (ii) comparison between AVS with ACTH stimulation and AVS without ACTH stimulation based on unsuccessful cannulation in both right and left adrenal veins; (iii) comparison of AVS with ACTH and AVS without ACTH based on unsuccessful cannulation of the left adrenal vein (LAV); (iv) comparison of AVS with ACTH and AVS without ACTH based on unsuccessful cannulation of the right adrenal vein (RAV).

Study quality and risk of bias assessment

The authors worked independently to search for and assess studies for their methodological quality. The Newcastle Ottawa scale (a valid instrument designed to assess the quality of cohort studies) was used to assess the methodological quality of included studies (21). The Newcastle-Ottawa scale assigns a maximum of four points for selection, two points for comparability, and three points for exposure or outcome. One point was awarded for each item present in the selection and outcome categories, and a maximum of two points was awarded for comparability. The scores of seven were considered high-quality studies and of five to six as moderate quality (21). Any disagreement in the study was resolved by consensus, and if necessary, a senior staff member was consulted.

Statistical analysis

OR with 95% CI were calculated to assess the effect of dichotomous data using Review Manager Version 5.3 software. I^2 and P values were calculated to assess the heterogeneity among studies ($I^2 > 50\%$ and $P < 0.1$ indicated substantial heterogeneity across studies) (22). Getdata software was used in case data were presented as a graph (23). The OR were pooled using only a random effects model to calculate a more conservative result. OR < 1 indicated a better outcome of AVS with ACTH stimulation, whereas OR > 1 indicated a worse outcome of AVS with ACTH stimulation.

Subgroup analyses were performed to compare the difference between pre- and post-ACTH stimulation for left and right adrenal vein cannulations. Sensitivity analyses were performed in studies with more stringent criteria (14, 16) for SI (≥2 or 3 for noncosyntropin-stimulated results and/or ≥5 for cosyntropin-stimulated results) and LI (≥2 for noncosyntropin-stimulated results and/or ≥4 for cosyntropin-stimulated results) to compare AVS with ACTH stimulation and AVS without ACTH stimulation based on incorrect lateralization.

Publication bias was not assessed as a result of the small number of studies in our meta-analysis. The Cochrane meta-analysis guidelines suggest the use of Egger's test for publication bias for analyses with >10 studies. $P < 0.05$ was considered to have a statistically significant difference in the outcomes between AVS with ACTH stimulation and AVS without ACTH stimulation.

Results

A total of 242 papers were retrieved from the four databases, among which 139 papers were duplicates. Three papers were recorded through reference list reviews, and 20 potential studies were ultimately included for full text view after reviewing the titles and abstracts. With further screening, a total of 14 studies met the inclusion criteria (4, 19, 20, 24–34). A flowchart of study selection is shown in Fig. 1. The main characteristics of eligible studies are summarized in Table 1. The publication dates of all included studies vary between January 1992 and March 2017.

Study characteristics

In eight studies, there was a comparison of AVS with ACTH stimulation and AVS without ACTH stimulation based on incorrect lateralization in patients with PA (19, 20, 24, 30–34). Of these eight studies, three used the more stringent criteria for SI and LI (20, 24, 34). In seven of the eight studies, success of surgery treatment was determined by factors, including biochemical cure (normalization of aldosterone/renin ratio and serum potassium), pathological findings, and /or clinical outcome (improvement in blood pressure and reduction in antihypertensive medications) (19, 20, 30–34). However, in one of the eight studies, it was assessed by multinomial regression modeling of peripheral and left adrenal vein sampling (24).

In seven studies, AVS with ACTH stimulation was compared with AVS without ACTH stimulation based on unsuccessful cannulations in both left and right adrenal veins (4, 20, 25–28, 31). In four other studies, there was a comparison between AVS with ACTH and AVS without ACTH based on unsuccessful cannulations of LAV or RAV (4, 19, 27, 29).

In all of the studies, intravenous bolus and/or infusion of 250 μg ACTH were administered (4, 19, 20, 24–34). However, in one study, an intermediate dose and a very low dose of ACTH were used in some patients (50 μg/hour and 250 pg IV, respectively) (19). The amount of time between ACTH administration and the collection of a second set of blood samples ranged between 15 and 30 minutes (4, 19, 20, 24–34).

Kline *et al.* (28) considered the SI > 3 as the benchmark for catheter placement among others. Therefore, it was also used in our analysis. Monticone *et al.* (4) considered the strict criteria to be of primary importance, and it was then considered in our analysis. In Satoh *et al.* (32), LI cutoff values of 3.5 before ACTH stimulation and 2.6 after ACTH stimulation presented higher

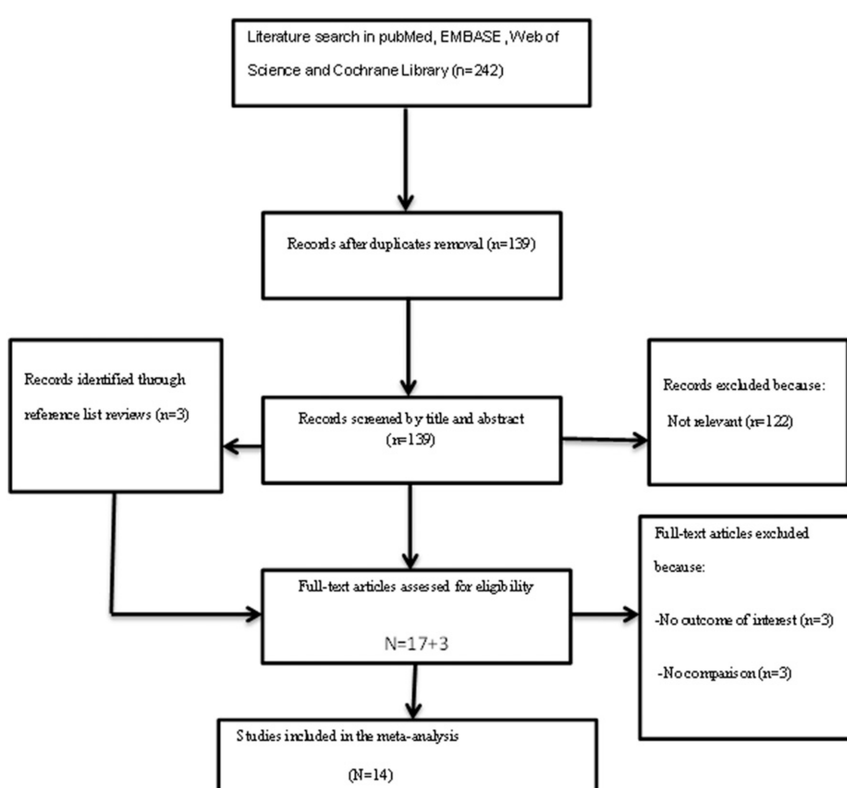

Figure 1. Flowchart of study selection.

Table 1. Characteristics of Included Studies

Reference	Study Design and Region	Period of Enrollment and/or Target Population	Method Groups and/or Sampling Technique	SI or SR		LI or LR		Sample Size, n
				Before ACTH	After ACTH	Before ACTH	After ACTH	
(4)	Cohort study in Italy and Japan	Patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	>3	>4	>4	>4	76
(20)	Cohort study in Australia	1 Year; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; sequential AVS	≥3	≥5	≥4	≥4	47
(24)	Cohort study in Montreal, Canada	From December 1989 to September 2015; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	?	≥5	≥2	≥4	188
(25)	Cohort study in Montreal, Canada	Between 1989 and 2014; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	≥2	≥5	≥2	≥4	175
(26)	Cohort study in Canada	10 Years; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	≥2	≥3	≥4	≥4	198
(27)	Cohort study in Canada	Patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	>3	>5	≥4	≥4	60
(28)	Cohort study in Canada	Between 1999 and 2005; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	>3	>3	?	?	63
(29)	Cohort study in Canada	Between June 2005 and July 2011; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	>3	>3	>3	>3	32
(30)	Cohort study in United States	Patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	>2	>2	≥4	≥4	114
(31)	Cohort study in Italy	Between 1988 and 2006; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	1.1–5	1.1–5	1.125–5	1.125–5	151
(32)	Cohort study in Japan	4.5 Years; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	≥1.1	≥1.1	≥3.5	≥2.6	87
(19)	Cohort study in Italy	From 2001 to 2007; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	≥1.1	≥1.1	≥2	≥2	67
(33)	Cohort study in Japan	Patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; sequential AVS	?	?	≥3	≥3	32
(34)	Cohort study in United States	Between 1991 and 2010; patients with PA having undergone AVS	AVS with ACTH vs AVS without ACTH; simultaneous bilateral AVS	>1.1	>5	>2	>4	108

Abbreviations: LR, lateralization ratio; SR, selectivity ratio; ?, unclear.

sensitivity and specificity than others. They were consequently considered in our analysis. In Rossi *et al.* (31), a cutoff value of two for LI and SI was used in our analysis, as the authors found that higher cutoffs may falsely decrease selectivity and lateralization. In Seccia *et al.* (19), a cutoff value of two for LI was chosen in our analysis, as it presented a higher number of correctly lateralized AVS among others.

Patient characteristics

The baseline characteristics, such as sample size, sex, age, plasma potassium, plasma aldosterone, plasma renin, antihypertensive, and blood pressure, were comparable between patients undergoing AVS with ACTH stimulation and patients undergoing AVS without ACTH stimulation.

There were no statistically significant differences between the patients in the two groups (group of AVS with ACTH stimulation and group of AVS without ACTH stimulation).

Publication bias

Risk of bias assessment for each study is summarized in Table 2. All included studies were considered to be of high quality.

Outcome

AVS with ACTH stimulation did not significantly reduce the number of incorrect lateralization compared with AVS without ACTH stimulation in patients with PA (OR: 0.76; 95% CI: 0.36, 1.59; $P = 0.47$). A substantial heterogeneity across studies was shown ($I^2 = 67\%$; $P = 0.003$). The same trend was found when analyzing the studies that used more stringent criteria for SI and/or LI (OR: 0.57; 95% CI: 0.29, 1.11; $P = 0.10$). The heterogeneity was not significant ($I^2 = 49\%$; $P = 0.14$; Fig. 2).

AVS with ACTH stimulation significantly reduced the number of unsuccessful cannulations of both adrenal veins more than AVS without ACTH stimulation in patients with PA (OR: 0.26; 95% CI: 0.17, 0.40; $P < 0.00001$). The heterogeneity was significant ($I^2 = 53\%$; $P = 0.05$; Fig. 3).

Table 2. Risk of Bias of the Studies

	Selection					Outcome			
Reference	Representativeness of Exposed Cohort	Selection of Nonexposed Cohort	Ascertainment of Exposure	Outcome Not Present at Baseline	Comparability of Cohorts (age, gender,…)	Assessment of Outcome	Sufficient Follow-Up Duration	Adequate Follow-Up	Total Score
(4)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(20)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(24)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(25)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(26)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	7
(27)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	7
(28)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	7
(29)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	7
(30)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(31)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8
(32)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(19)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(33)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
(34)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9

AVS with ACTH stimulation reduced the number of unsuccessful cannulations of LAV more than AVS without ACTH stimulation in patients with PA. There was a statistically significant difference (OR: 0.14; 95% CI: 0.06, 0.33; $P < 0.00001$). The heterogeneity between studies was not significant (I^2 = 27%; P = 0.25; Fig. 4).

AVS with ACTH stimulation significantly reduced the number of unsuccessful cannulations of RAV more than AVS without ACTH stimulation in patients with PA (OR: 0.30; 95% CI: 0.12, 0.71; P = 0.007). The substantial heterogeneity was shown (I^2 = 71%; P = 0.02; Fig. 5).

Discussion

The results of this meta-analysis show that in patients with PA, AVS with ACTH stimulation does not significantly reduce the number incorrect lateralization more than AVS without ACTH stimulation (Fig. 2). However, AVS with ACTH stimulation significantly reduces the number of unsuccessful cannulations more than AVS without ACTH stimulation (Figs. 3–5).

AVS procedure, with or without ACTH stimulation, is still a controversial debate. In fact, many studies have been recently conducted and compared AVS with ACTH stimulation and AVS without ACTH stimulation in patients with PA (24, 29–31, 34). Some studies found that AVS with ACTH stimulation is more beneficial, whereas others did not (19, 30–32).

Seccia *et al.* (19) found that the improvement in the ascertainment of selectivity occurring with ACTH stimulation was overridden by the confounding effect on identification of lateralized aldosterone excess. The same authors did not then support the systematic use of ACTH

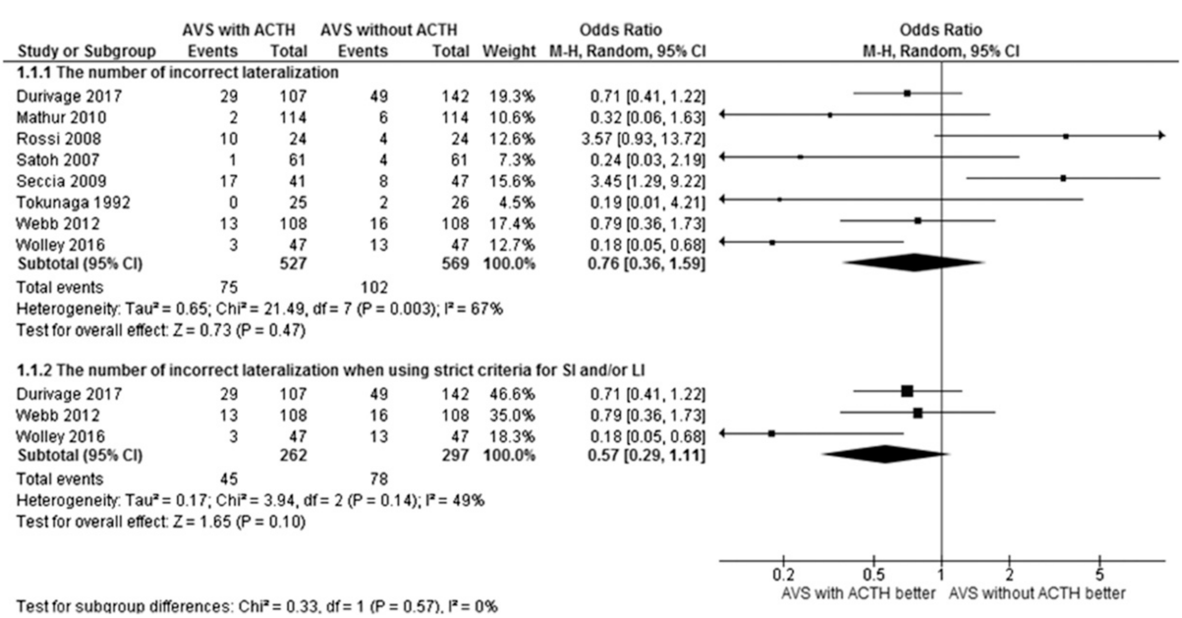

Figure 2. Forest plot: number of incorrect lateralization of AVS with ACTH stimulation in comparison with AVS without ACTH stimulation.

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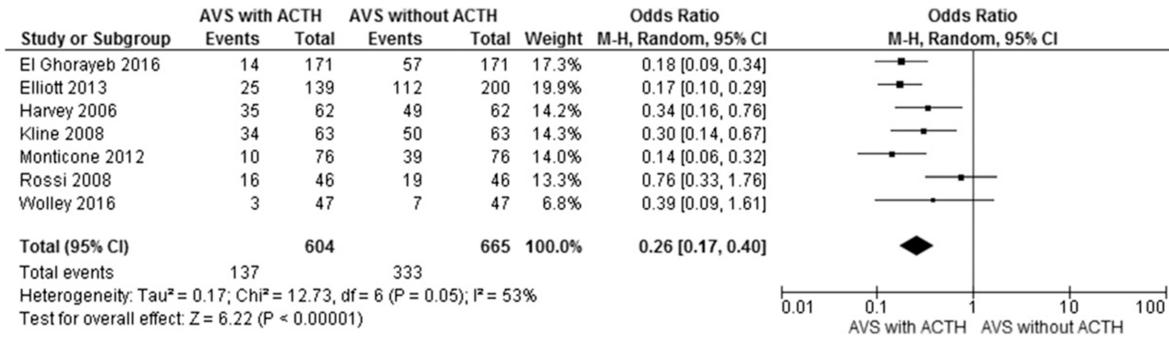

Figure 3. Forest plot: number of unsuccessful cannulations in both adrenal veins when comparing AVS with ACTH stimulation and AVS without ACTH stimulation.

stimulation. Rossi *et al.* (31) similarly concluded that the improved selectivity rate provided by ACTH stimulation should be weighed against the loss of correct lateralization. However, the results of our meta-analysis showed that ACTH stimulation reduced the number of incorrect lateralization even though there was no statistically significant difference. Therefore, the loss of correct lateralization has not been proven.

On the other hand, Wolley *et al.* (20) found that the proportion of diagnostic studies was higher after ACTH, as a result of both slightly more AVS procedures achieving bilateral successful cannulation but also a result of the attainment of a diagnostic result in cases where the unstimulated AVS had been inconclusive. However, the authors failed to find a substantial difference in the selectivity rate.

Marthur *et al.* (30) found that although the majority of patients can successfully be lateralized with only pre-ACTH stimulation values, the most accurate methods for AVS lateralization are post-ACTH stimulation. Therefore, our results correlate with their findings. In fact, we found that AVS with ACTH stimulation can reduce the number of incorrect lateralization more than AVS without ACTH stimulation, although the difference was not statistically significant (Fig. 2). The reason may be the slightly more AVS procedures achieving bilateral cannulation after ACTH stimulation (20). However, this is in contradiction with our findings. In fact, we did find substantial AVS procedures achieving bilateral cannulation after ACTH stimulation.

Nevertheless, Kline *et al.* (29) demonstrated that those so-called unsuccessful catheter placements before ACTH stimulation are probably actually quite successful in the hands of an experienced operator. The same authors concluded that ACTH infusion may help less-experienced AVS operators to obtain clinically useful results by maximizing the recognition of successful sampling. Therefore, for experienced centers, the two techniques (AVS with ACTH stimulation and AVS without ACTH stimulation) may be almost the same. This is supported by a recent study by Monticone *et al.* (4) who demonstrated that cosyntropin infusion may be of help for those centers with low rates of successful cannulation and perform at least as well as the unstimulated protocol for the final diagnosis of PA subtypes. This could lead us to conclude again that ACTH stimulation may be more useful for inexperienced centers to minimize failure rates of cannulation. However, this would need further verification.

We highlighted that different cut-off values of SI and LI were used in the studies included (Table 1). Of the studies included, some used less-permissive criteria for SI and LI. However, many experts and/or recent guideline recommend more strict criteria for SI and LI. A higher cutoff for SI (at least two or three for nonstimulated results and/or five for ACTH-stimulated results) or LI (two for basal results and/or four for ACTH-stimulated results) is usually advised (14, 16, 25, 35). Afterward, we conducted sensitivity analyses, including only the studies with more strict criteria for SI and LI (20, 24, 34). A reduction in the number of incorrect lateralizations

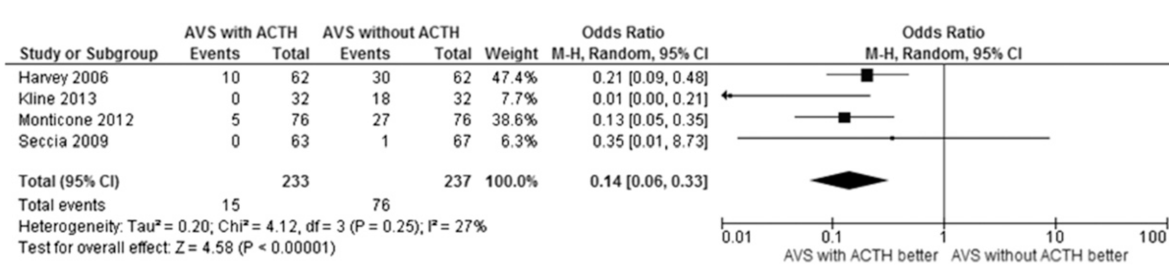

Figure 4. Forest plot: number of unsuccessful cannulations of LAV when comparing AVS with ACTH stimulation and AVS without ACTH stimulation.

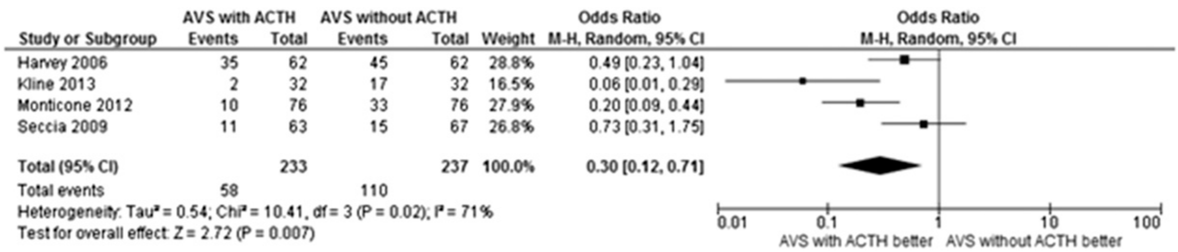

Figure 5. Forest plot: number of unsuccessful cannulations of RAV when comparing AVS with ACTH stimulation and AVS without ACTH stimulation.

became more prominent after ACTH stimulation. However, there was not also a statistically significant difference (Fig. 2). Thus, the sensitivity analyses strengthened our findings.

This meta-analysis showed that AVS with ACTH stimulation significantly reduces the number of unsuccessful cannulations. It also showed that AVS with ACTH stimulation tends to reduce the number of incorrect lateralization when compared with AVS without ACTH stimulation. However, ACTH stimulation has advantages and disadvantages. The advantages are that ACTH (1–24) infusion maximizes the cortisol gradient between the adrenal and peripheral veins and minimizes aldosterone fluctuations (14). It can also selectively enhance aldosterone secretion by adenomas. Indeed, aldosterone secretion by adenomas is usually partially ACTH dependent (36).

ACTH stimulation may have disadvantages of enhancing aldosterone secretion from the suppressed contralateral adrenal in a patient with a unilateral adenoma or enhancing a difference between two hyperplastic glands (4, 14, 19, 37). On the other hand, surgical outcome (correct or incorrect lateralization) after adrenalectomy is usually determined by factors, such as clinical outcome, pathology outcome, and/ or biochemical outcomes (27, 29). However, the determination of outcome after adrenalectomy for PA had been severely limited by a lack of standardized definitions of what constitutes cure and how to report changes in biochemistry, blood pressure, and total dosage of antihypertensive medications until the recent publication of an international consensus (Primary Aldosteronism Surgical Outcome) (38, 39). Length of follow up necessary to document a long-term, durable cure also lacked standardization (38). In addition, studies using clinical, pathological, and biochemical outcome after adrenalectomy to determine the best AVS methods and indexes may have substantial verification and inclusion biases. In fact, given that these studies are based on patient progress after adrenalectomies were performed, according to AVS results, it is difficult to evaluate how patients who had been denied surgery based on AVS results would have done if they had been submitted to adrenalectomy (24).

Our present study has several limitations. First, variability in institutional protocols for performing the procedure, shortage of expert interventional radiologists trained in this procedure, pitfalls in technique, and strategies to improve success are still the main challenges (40). In addition, the patients included in the studies were seen over the 15 years, and obviously, different assays for the measurement of cortisol and aldosterone may have been used over years. Therefore, SI and LI cut-off values may have been subject to change. This can affect the pooled results of this meta-analysis. Second, any potential benefits of ACTH stimulation need to be assessed against its cost. As a result of the limited number of studies and the absence of cost analysis in these studies, we are unable to analyze the cost effectiveness of using ACTH in all AVS procedure. Finally, the studies were mostly small in sample size and retrospective in design. Therefore, the results of this meta-analysis are not conclusive or generalizable.

In conclusion, the results of this meta-analysis showed that AVS with ACTH stimulation can significantly reduce the number of unsuccessful cannulations more than AVS without ACTH stimulation. However, according to our findings, the number of incorrect lateralization is similar between the two techniques. Larger prospective studies should be conducted to verify our findings and resolve the dilemma of ACTH or no ACTH in AVS.

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