Consequences of Adrenal Venous Sampling in Primary Hyperaldosteronism and Predictors of Unilateral Adrenal Disease

Aarti Mathur, MD, Clinton D Kemp, MD, Utpal Dutta, MD, Smita Baid, MD, Alejandro Ayala, MD, Richard E Chang, MD, Seth M Steinberg, PhD, Vasilios Papademetriou, MD, Eileen Lange, RN, CCRP, Steven K Libutti, MD, FACS, James F Pingpank, MD, FACS, H Richard Alexander, MD, FACS, Giao Q Phan, MD, Marybeth Hughes, MD, FACS, W Marston Linehan, MD, Peter A Pinto, MD, Constantine A Stratakis, MD, D(Med)Sci, Electron Kebebew, MD, FACS

BACKGROUND: In patients with primary hyperaldosteronism, distinguishing between unilateral and bilateral adrenal hypersecretion is critical in assessing treatment options. Adrenal venous sampling (AVS) has been advocated by some to be the gold standard for localization of the responsible lesion, but there remains a lack of consensus for the criteria and the standardization of technique.

STUDY DESIGN: We performed a retrospective study of 114 patients with a biochemical diagnosis of primary hyperaldosteronism who all underwent CT scan and AVS before and after corticotropin (ACTH) stimulation. Univariate and multivariate analyses were performed to determine what factors were associated with AVS lateralization, and which AVS values were the most accurate criteria for lateralization.

RESULTS: Eighty-five patients underwent surgery at our institution for unilateral hyperaldosteronism. Of the 57 patients who demonstrated unilateral abnormalities on CT, AVS localized to the contralateral side in 5 patients and revealed bilateral hyperplasia in 6 patients. Of the 52 patients who showed bilateral disease on CT scan, 43 lateralized with AVS. The most accurate criterion on AVS for lateralization was the post-ACTH stimulation value. Factors associated with AVS lateralization included a low renin value, high plasma aldosterone-to plasma-renin ratio, and adrenal mass $\geq$ 3 cm on CT scan.

CONCLUSIONS: Because 50% of patients would have been inappropriately managed based on CT scan findings, patients with biochemical evidence of primary hyperaldosteronism and considering adrenalectomy should have AVS. The most accurate measurement for AVS lateralization was the post-ACTH stimulation value. Although several factors predict successful AVS lateralization, none are accurate enough to perform AVS selectively. (J Am Coll Surg 2010;211:384–390. © 2010 by the American College of Surgeons)

The prevalence of primary hyperaldosteronism in the hypertensive population can be as high as 15%.[1,2] The majority of patients with primary hyperaldosteronism have either idiopathic bilateral hyperplasia or an aldosterone-producing adenoma. Other rare causes include unilateral hyperplasia, aldosterone-producing adrenocortical carcinoma, aldosterone-producing ovarian tumor, or familial hyperaldosteronism including glucocorticoid-remediable hyperaldosteronism.[3,4]

The goal of treatment is to minimize morbidity and mortality from aldosterone excess, which can result in ad-

Disclosure Information: Nothing to disclose.

This research was supported by the Intramural Research Program of the NIH, National Cancer Institute, Center for Cancer Research.

Received March 5, 2010; Revised May 4, 2010; Accepted May 11, 2010.

From the Endocrine Oncology Section, Surgery Branch (Mathur, Kemp, Phan, Hughes, Kebebew), the Biostatistics and Data Management Section, Office of the Clinical Director, Center for Cancer Research (Steinberg), and the Urologic Oncology Branch (Linehan, Pinto), National Cancer Institute; the Department of Diagnostic Radiology, Warren F Magnuson Clinical Center (Chang); and the Program on Developmental Endocrinology and Genetics, Eunice Kennedy Shriver National Institutes of Child Health and Human Development (NICHD) (Dutta, Baid, Ayala, Lange, Stratakis); the Veterans Administration and Georgetown University, Washington DC (Papademetriou); the Department of Surgery, Montefiore Medical Center and the Albert Einstein College of Medicine, Bronx, NY (Libutti); the Division of Surgical Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, PA (Pingpank); and the Department of Surgery, Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, MD (Alexander).

Correspondence address: Electron Kebebew, MD, FACS, National Cancer Institute Surgery Branch CRC, Room 4-5952, 10 Center Dr, MSC 1201, Bethesda, MD 20892-1201.

ISSN 1072-7515/10/$36.00
doi:10.1016/j.jamcollsurg.2010.05.006

Abbreviations and Acronyms

AC = aldosterone-to-cortisol ratio
ACTH = corticotropin
AVS = adrenal venous sampling
PAC = plasma aldosterone concentration
PRA = plasma renin activity

verse cardiovascular events independent of high blood pressure.[5] Therefore, in patients with primary hyperaldosteronism, distinguishing between unilateral and bilateral adrenal hypersecretion is critical in assessing treatment options. Diagnosis of unilateral hyperplasia or an aldosterone-producing adenoma may be amenable to surgical cure with a unilateral adrenalectomy; a diagnosis of idiopathic bilateral hyperplasia should be managed with a mineralocorticoid receptor antagonist.[6]

Adrenal venous sampling (AVS) was introduced in the late 1960s as a test to differentiate unilateral from bilateral hyperaldosteronism.[7] Because of technical difficulties in cannulating both adrenal veins, and improved imaging modalities such as CT and MRI, AVS was not widely adopted. Although sensitivities with CT scan have been reported to be as high as 90%, recent studies highlight the pitfalls of noninvasive imaging techniques, causing some to now advocate AVS as the gold standard for lateralization.[1,4,8-11] In a prospective study of 203 patients by Young and colleagues,[4] 21.7% of patients would have been incorrectly excluded as candidates for adrenalectomy and an additional 24.7% may have had an unnecessary or inappropriate adrenalectomy based on CT scan findings alone. In a meta-analysis of 950 patients by Kempers and associates,[12] 37.8% of patients had CT or MRI results that were discordant with AVS. If only CT or MRI had been used, inappropriate adrenalectomy would have taken place in 14.6% of patients, inappropriate exclusion of adrenalectomy would have occurred in 19.1%, and incorrect side adrenalectomy in 3.9%. Zarnegar and colleagues[13] found that CT scan can reliably diagnose adenomas larger than 1.0 cm and that AVS should be used selectively, when CT findings are either equivocal or both adrenal glands are abnormal.[13]

Although AVS may be re-emerging as the gold standard for differentiating between unilateral and bilateral primary hyperaldosteronism, there is a lack of standardization of technique and limited data on which AVS values to use to distinguish between unilateral and bilateral disease.[8-11,13-15] The aims of this study were to determine if routine AVS is necessary in all patients, what factors predict AVS lateralization, and what technique for AVS should be used to determine lateralization.

METHODS

Patients

A computerized medical record database was used to identify 114 patients with the diagnosis of primary hyperaldosteronism who underwent CT scan and AVS under a clinical protocol approved by our Institutional Review Board. Medical records were retrospectively reviewed to obtain baseline demographic data, laboratory values, CT scan and AVS reports, pathology reports, and operative reports. All patients had comprehensive biochemical testing to confirm the diagnosis of primary hyperaldosteronism. In addition to aldosterone and renin levels, patients had confirmatory testing including a sodium chloride loading test, a captopril test, or a posture test. Clinical outcomes data included systolic and diastolic blood pressure, potassium level, aldosterone level, and number of antihypertensive medications at postoperative follow-up. Follow-up was performed either in the clinic or by telephone interview with the patient.

Adrenal venous sampling technique

Regardless of CT scan findings, all patients underwent AVS, which was performed by experienced interventional radiologists. Venous catheters were introduced via both femoral veins. Simultaneous catheterization of bilateral adrenal veins was performed in all patients using 4-F Mickaelsson, Simmons 1, and Cobra 2 catheters with or without modifications, to sample the right adrenal vein; and 4-F Simmons 2 or 3 catheters and, rarely, a sub 3-French microcatheter to obtain samples from the left adrenal vein. Peripheral samples were obtained from the right iliac vein. Two sets of baseline blood samples were drawn 5 minutes apart from each adrenal vein and the iliac vein. After the baseline draws, an intravenous bolus of 0.25 mg of ACTH followed by an infusion of ACTH (0.25 mg in 250 mL normal saline) at a rate of 150 mL/hour was administered. Blood samples were collected at 5 minutes, 10 minutes, and 15 minutes post-ACTH infusion, and levels for aldosterone and cortisol were measured. Appropriate placement of catheters in the adrenal veins was surmised by contrast venography and subsequently confirmed by appropriately elevated cortisol levels in the adrenal vein samples as compared with levels in the peripheral samples (ratio > 2).

Sample interpretation

The aldosterone-to-cortisol ratio (AC) was computed for each sample to correct for varying capture and dilution of adrenal venous effluent. Patients who demonstrated unilateral hypersecretion of aldosterone were referred for an adrenalectomy. Diagnosis of a unilateral hyperfunctioning adrenal gland was made if the AC ratio on one side was at

least 4 times greater than on the contralateral side and the peripheral samples. An AC ratio that was lower than the periphery on the unaffected side especially after stimulation suggested a suppressed gland, and therefore, a unilateral hyperfunctioning gland on the contralateral side. Diagnosis of bilateral hyperplasia was made if the AC ratios on both sides were elevated and the response to stimulation was similar with no gradient observed between the 2 sites. Twelve different ratios were derived from the aldosterone and cortisol levels pre- and post-ACTH stimulation for each side at the time intervals stated above. These were an AC ratio for each side, ratio of AC from one gland versus peripheral AC, and greater AC ratio from one gland versus the smaller AC ratio from the contralateral gland.

Statistical methods

The association between CT and AVS was determined by cross-classifying the 2 parameters. The initial screening to determine which ratios were associated with AVS lateralization to left versus right side was performed using a Wilcoxon rank sum test. The p values presented are 2-sided and have not been adjusted for multiple comparisons. Ratios found to be statistically different according to left versus right location of abnormality were further evaluated for their ability to classify correctly according to side individually, in pairs based on time of determination, and then jointly, using logistic regression analysis. The Mann-Whitney rank sum, or Kruskal-Wallis tests were used to identify factors associated with AVS lateralization. Statistical analysis was performed using standard statistical software (SAS, Inc).

RESULTS

Of 114 patients, 85 underwent adrenalectomy at our institution for unilateral hyperaldosteronism. The demographic and clinical data are summarized in Table 1. Our group of 114 patients consisted of 63 men and 51 women with mean age of 50.6 years (range 3 to 73 years). The mean plasma aldosterone concentration was 41.1 ng/dL (range 2 to 328 ng/dL), mean plasma renin activity value was 0.9 ng/mL (range 0.1 to 23 ng/mL), and mean plasma aldosterone concentration-to-plasma renin activity (PAC/PRA) ratio was 100 (range 7 to 640). Patients with a PAC/PRA of less than 14 ng/dL had aldosterone levels greater than 30 ng/dL, and all patients had confirmatory testing with a sodium chloride loading test, a captopril test, or a postural test. The average duration of hypertension was 12.8 years and ranged from several months to a maximum of 40 years. Patients were on an average of 2 to 3 antihypertensive medications. The average creatinine and body mass index were 1.1 mg/dL (range 0.5 to 2.3 mg/dL) and 30.6 kg/m^2 (range 19 to 47 kg/m^2), respectively (Table 1).

Table 1. Study Cohort Demographics and Clinical Characteristics

Demographic/characteristic	Data
Age, y	
Mean age ± SD, y	50.6 ± 11.0
Gender, n	
Male	63
Female	51
Duration of hypertension, y	12.8 ± 8.9
Antihypertensive medications used, n	2.7 ± 1.3
Potassium, mmol/L (reference range 3.3–5.1 mmol/L)	3.2 ± 0.5
Creatinine, mg/dL (reference range 0.9–1.4 mg/dL)	1.1 ± 0.3
Body mass index, kg/m^2	30.6 ± 6.1
Aldosterone, ng/dL (reference range ≤ 21 ng/dL)	41.4 (2–328)
Renin, ng/mL (reference range 0.6–3 ng/mL)	0.92 (0.1–23)
Aldosterone/renin ratio	99.6 (7–640)
Largest diameter on CT scan, cm	2.4 ± 1.6
History of MI/CHF, n	11
History of CVA/TIA, n	8
History of thyroid dysfunction, n	12
Family history of endocrinopathy, n	
Thyroid dysfunction	8
Hyperaldosteronism	4

Data are presented as mean ± SD unless otherwise stated.
CHF, congestive heart failure; CVA, cerebrovascular accident; MI, myocardial infarction; TIA, transient ischemic attack.

Twelve patients had a previous history of thyroid dysfunction. Eleven patients had a history of myocardial infarction or congestive heart failure, and 8 patients had suffered an earlier cerebrovascular event or transient ischemic attack. Four patients had a first degree relative with primary hyperaldosteronism.

Both adrenal veins were catheterized successfully in all patients based on venography and elevated cortisol values compared with values from the periphery. Two patients had to have repeat procedures secondary to misplaced blood samples. One patient developed severe lumbar back pain that spontaneously resolved after an AVS procedure without radiographic evidence of adrenal hemorrhage or infarction. There were no other adverse events from AVS.

CT and AVS results

Of 57 patients who had a unilateral abnormality on CT scan, 5 patients lateralized to the contralateral side by AVS, and 6 patients had AVS consistent with bilateral hyperplasia (Fig. 1). Therefore, 19.3% of patients would have had either an unnecessary adrenalectomy or adrenalectomy of the nonfunctioning adrenal gland if AVS was not performed. In 52 patients who showed bilateral disease on CT

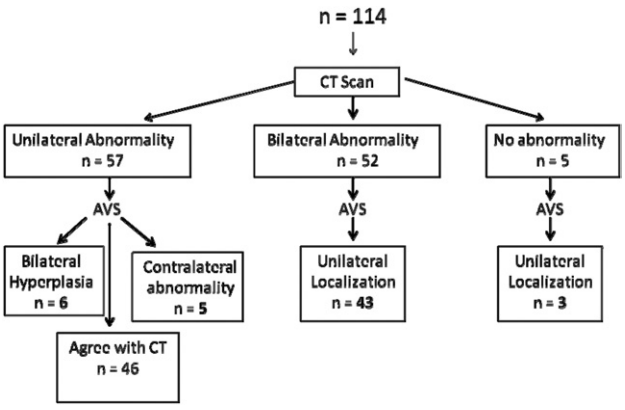

Figure 1. Flow diagram of study cohort and localization by CT and adrenal venous sampling (AVS). Fifty percent of patients would have been inappropriately managed based on CT findings alone.

scan, AVS lateralized to one side in 43 patients and was concordant with the CT scan in 9 patients. In 5 patients who had no abnormality on CT scan, 3 lateralized with AVS. Of the group of 114 patients, 57 patients (50%) would have been inappropriately managed based on CT scan findings alone.

Aldosterone-to-cortisol criteria for AVS lateralization

Logistic regression analysis, including the above listed AC ratios pre- and post-ACTH stimulation, showed that although 98% of patients could be lateralized based on the post-ACTH stimulation AC ratios with evidence of suppression of the contralateral gland from the periphery, 95% of patients could be lateralized with only pre-ACTH stimulation values (Table 2). The remaining 2% did not localize with AVS. The adrenal vein AC ratio on each side and the ratio of adrenal AC to periphery AC on each side were adequate for successful lateralization.

Factors predicting lateralization

In our group of 114 patients, 17 patients were not localized with AVS, indicating bilateral hyperplasia and the need for further medical management. Univariate analyses were performed to assess which factors may predict lateralization with AVS (Table 3). Age, gender, PAC, creatinine, body mass index, duration of hypertension, number of antihypertensive medications, and ability to localize an enlarged adrenal gland or mass on CT were not associated with lateralization by AVS. However, PRA, PAC:PRA ratio, and size of a nodule on CT scan greater than or equal to 3 cm were significantly associated with detection of unilateral disease by AVS ($p \leq 0.02$) (Fig. 2).

Surgical outcomes

Of the 114 patients, 85 patients underwent surgery at our institution. Thirty-three patients had right adrenalectomy, and 51 patients had left adrenalectomy. One patient was identified as having massive macronodular adrenocortical disease and underwent bilateral adrenalectomy. Eighteen patients underwent open adrenalectomy and 67 patients had a laparoscopic adrenalectomy. Twenty patients experienced perioperative complications (Table 4). One patient had an intraoperative diaphragmatic injury and required placement of a chest tube. Another patient had a Mallory Weiss tear that was postoperatively identified and emboli-

Table 2. Aldosterone-to-Cortisol Ratio Criteria for Adrenal Venous Sampling Lateralization

Ratio	AVS lateralized to right	AVS lateralized to left	p Value
Pre-ACTH stimulation			
AC right	126.70 ± 88.79	3.71 ± 0.68	<0.0001
AC left	27.83 ± 21.92	33.26 ± 5.97	<0.0001
AC peripheral	6.76 ± 2.64	4.95 ± 0.78	0.26
AC right:AC peripheral	22.82 ± 6.04	1.31 ± 0.27	<0.0001
AC left:AC peripheral	3.20 ± 1.12	10.7 ± 1.95	<0.0001
AC larger:AC smaller	23.57 ± 5.17	13.84 ± 2.14	0.67
Post-ACTH stimulation			
AC right	22.32 ± 3.01	16.82 ± 15.18	<0.0001
AC left	12.71 ± 10.75	31.95 ± 9.53	<0.0001
AC peripheral	3.32 ± 0.56	3.90 ± 0.64	0.62
AC right:AC peripheral	8.71 ± 1.25	1.30 ± 0.61	<0.0001
AC left:AC peripheral	1.67 ± 0.65	8.95 ± 2.30	<0.0001
AC larger:AC smaller	24.99 ± 6.56	34.7 ± 10.03	0.83

Patients were divided into 2 groups based on which side they lateralized to by AVS. Mean values for each ratio are separately recorded for patients who lateralized to the left side versus the right side. Data are reported as mean ± standard error of the mean.
AC, aldosterone-to-cortisol ratio; ACTH, corticotrophin; AVS, adrenal venous sampling.

Table 3. Factors Predictive of Lateralization by Adrenal Venous Sampling

Factor	Lateralized	Not lateralized	p Value
Gender, %			
Male	56	53	0.61
Female	44	47	
Age ± SEM, y	50.6 ± 1.0	52.9 ± 0.16	0.21
Aldosterone, ng/dL	38.5 ± 3.7	45.7 ± 19.5	0.19
Renin, ng/mL	0.93 ± 0.03	0.87 ± 0.16	0.01
PAC:PRA	102.6 ± 13.4	61.9 ± 30.5	0.02
Potassium, mmol/L	3.2 ± 0.1	3.3 ± 0.1	0.77
Creatinine, mg/dL	1.1 ± 0.03	1.0 ± 0.04	0.84
Body mass index, kg/m^2	30.6 ± 0.6	31.3 ± 1.5	0.58
Duration of hypertension, y	12.8 ± 0.9	12.8 ± 2.2	0.75
Antihypertensives used, n	2.8 ± 0.1	2.4 ± 0.3	0.19
CT lateralization, %	52.6	35.3	0.20
Size on CT scan ≥ 3 cm, n	5	0	<0.0001

Mean values are presented for patients who either lateralized or did not lateralize by AVS. Data are reported as mean ± SD or SE of the mean.
AVS, adrenal venous sampling; PAC, plasma aldosterone concentration; PRA, plasma renin activity.

zed. The remaining patients had grade 1 and 2 complications. There were no perioperative deaths.

Final pathologic findings confirmed a solitary cortical adenoma in 76% of patients and an additional 14% of patients had an adenoma within the background of cortical hyperplasia. Average adenoma size was 1.58 ± 0.81 cm (range 0.2 to 4.5 cm). Seven patients had nodular hyperplasia, and in one patient, no nodule was identified. This patient had persistent symptoms postoperatively, underwent further workup, and ultimately had a contralateral adrenalectomy likely secondary to a mislateralization. Her previous post-ACTH AC ratio from the initial AVS was 48 and lateralized to the left adrenal gland. Pathology reports could not be located for 7 patients. Eighty of 85 patients were either cured or had improved symptom control as evidenced by normal postoperative PAC levels or improvement or normalization of blood pressure. Postoperative aldosterone levels were available and normal in 27 patients. At postoperative follow-up, 17 patients were normotensive (blood pressure < 140/90 mmHg) completely off all of their preoperative blood pressure medications, and 48 patients were on less medication. The average reduction in blood pressure medication was 1.5 medications, with a range of 1 to 3 medications discontinued per patient. Fifteen patients were on the same number of medications, but now were normotensive. All but one patient came off potassium supplementation because of persistent disease. Median follow-up was 8.8 months, with a range from 1 month to 9 years.

DISCUSSION

The results of this study support the routine use of AVS in all patients with biochemical evidence of primary hyperal-

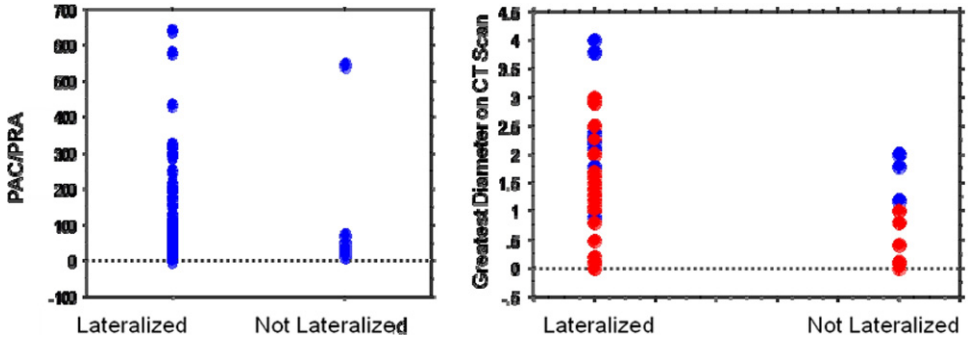

Figure 2. Scattergram showing the range of values for mean plasma aldosterone concentration-to-plasma renin activity (PAC/PRA) and greatest tumor diameter (cm) of lesion on CT scan versus patients who lateralized or did not lateralize by adrenal venous sampling. Blue and red dots refer to size of lesions on right and left sides, respectively.

Table 4. Postoperative Complications

Complication	n
Fever with spontaneous resolution	5
Pneumonia treated with antibiotics	3
Arrhythmias/premature ventricular contractions	3
1 episode of hemoptysis	1
Mallory Weiss tear requiring embolization	1
Pancreatitis	2
Transaminitis	1
Prolonged ileus	2
Acute renal failure not requiring dialysis	2
Redman's syndrome from preoperative vancomycin	1
Intraoperative diaphragmatic injury	1
Hyperkalemia	2
Herpes labialis	1

dosteronism because 50% of patients would have been inappropriately managed based on CT scan findings alone. Moreover, the most accurate measurement for AVS lateralization was the post-ACTH stimulation AC ratio, although a majority of patients can be localized without ACTH stimulation. We also found several factors associated with successful AVS lateralization such as absolute renin value, aldosterone-to-renin ratio, and size of the lesion on CT scan, but none were accurate enough to forgo the need for AVS.

Traditionally, AVS has been considered a complex procedure associated with morbidities. The procedure itself is technically challenging and requires an experienced interventional radiologist. Historically, samples from the right adrenal vein could not be obtained in 30% of patients and complications such as bilateral adrenal infarction, adrenal vein dissection, and adrenal hemorrhage led to the use of CT and MRI as preferred methods to distinguish between unilateral and bilateral adrenal disease.[16] However, even high-resolution, thin-section (2 to 3 mm) CT scans can miss small nodules and can also pick up small nonfunctional incidentalomas. Our findings support the routine use of AVS in all patients with biochemical evidence of primary hyperaldosteronism because half of the patients would have been inappropriately managed based on CT findings alone. There were no technical complications associated with AVS in our study and our morbidity rate was 2.6%. Two patients required repeat AVS because a clerical error resulted in misplaced blood samples and one patient developed severe lumbar back pain that spontaneously resolved without radiographic evidence of adrenal hemorrhage or infarction.

No general consensus on the technique for AVS, the AC measurements taken, and the criteria used (with and without ACTH stimulation) for lateralization exists. Although some investigators use sequential adrenal vein catheterization, others use simultaneous sampling of both adrenal veins. The decision to use ACTH for adrenal gland stimulation, the dose, and method of administration also vary across institutions. One of the strengths of our study is that AVS has been performed with a consistent and systematic protocol by experienced radiologists. At our institution, AVS is performed by simultaneous catheterization of bilateral adrenal veins with and without ACTH stimulation given as a bolus and continuous infusion. However, on univariate and multiple logistic regression analyses of 12 different ratios derived from the AC ratio, pre-ACTH stimulation values successfully lateralized in 95% of patients, and the addition of ACTH allowed 98% of patients to lateralize. ACTH stimulation was the most accurate method for lateralization; it also allows for confirmation of successful adrenal vein cannulation and minimizes variability in cortisol secretion during sampling.

Factors that predicted successful AVS lateralization in univariate analyses included a low absolute renin value, high PAC/PRA, and lesion size on CT scan greater than or equal to 3 cm. We are not aware of any studies that have addressed predictive factors for successful AVS lateralization using demographic, clinical, laboratory, and imaging data. It is not surprising to find that patients with a unilateral large adrenal mass on preoperative CT scan were more likely to have AVS lateralize the tumor, especially in the setting of a normal contralateral adrenal gland. None of these factors, however, in combination or alone, could reliably predict unilateral hyperaldosteronism because the false positive rate of CT scan lateralization was 19%.

Previous studies have shown that unilateral adrenalectomy in patients with an aldosteronoma or unilateral hyperplasia results in complete surgical cure, with normalization of blood pressure without the use of antihypertensives in about one-third of patients and improvement in blood pressure in the remaining patients.[15,16] Hypokalemia can be reversed in up to 100% of patients. Factors predictive of complete surgical cure include duration of hypertension less than 6 years, less than 3 antihypertensives to control blood pressure preoperatively, younger age (less than 50 years old), and female gender.[17,18] In this study, our surgical cure rate was slightly less than what has been previously reported in the literature. This may be due to a longer duration of hypertension (12.9 years) in our study cohort, and the fact that 54% of patients were on 3 or more antihypertensives. Nonetheless, all the patients who had PAC levels available postoperatively had normal or undetectable levels. A majority of patients derived benefit from their operation in terms of hypokalemia resolution and number of blood pressure medications required. Postoperatively, patients were on an average of 1.5 blood pressure medications (range 0 to 6 medications).

The main limitation of our retrospective study is that our study cohort may not be reflective of most patients with primary hyperaldosteronism because we are a referral center.

However, because all patients underwent a comprehensive biochemical workup to confirm the diagnosis of primary hyperaldosteronism and underwent a systematic approach for lateralization with both AVS and CT scanning in all cases, we believe our findings address the controversial issues of performing routine AVS, and determining if any clinical, imaging, and laboratory criteria can be used to avoid the need for AVS.

In conclusion, distinguishing between unilateral and bilateral adrenal hypersecretion in patients with primary hyperaldosteronism is critical in assessing treatment options. This study supports the routine use of AVS in patients with biochemical evidence of primary hyperaldosteronism and who want to proceed with adrenalectomy. Although the majority of patients can successfully be lateralized with only pre-ACTH stimulation values, the most accurate method for AVS lateralization is with ACTH stimulation. Furthermore, using renin values, PAC/PRA ratios, and size of the lesion on CT scan may guide the clinician in determining which patients will successfully lateralize with AVS, but none of these predictive factors are accurate enough to determine which patients need AVS.

Author Contributions

Study conception and design: Mathur, Kemp, Dutta, Baid, Ayala, Chang, Stratakis, Kebebew

Acquisition of data: Mathur, Kemp, Dutta, Baid, Ayala, Chang, Steinberg, Papademetriou, Lange, Libutti, Pingpank, Alexander, Phan, Hughes, Linehan, Pinto, Stratakis, Kebebew

Analysis and interpretation of data: Mathur, Kemp, Dutta, Baid, Ayala, Chang, Steinberg, Papademetriou, Lange, Libutti, Pingpank, Alexander, Phan, Hughes, Linehan, Pinto, Stratakis, Kebebew

Drafting of manuscript: Mathur, Kemp, Dutta, Baid, Ayala, Chang, Steinberg, Papademetriou

Critical revision: Mathur, Baid, Chang, Steinberg, Papademetriou, Libutti, Alexander, Phan, Hughes, Linehan, Pinto, Stratakis, Kebebew

REFERENCES

1. McKenzie TJ, Lillegard JB, Young WF Jr, Thompson GB. Aldosteronomas—state of the art. Surg Clin North Am 2009; 89:1241–1253.
2. Mulatero P, Stowasser M, Loh KC, et al. Increased diagnosis of primary aldosteronism, including surgically correctable forms, in centers from five continents. J Clin Endocrinol Metab 2004; 89:1045–1050.
3. Young WF Jr. Minireview: primary aldosteronism-changing concepts in diagnosis and treatment. Endocrinology 2003;144: 2208–2213.
4. Young WF Jr, Stanson AW, Thompson GB, et al. Role for adrenal venous sampling in primary aldosteronism. Surgery 2004; 136:1227–1235.
5. Milliez P, Girerd X, Plouin PF, et al. Evidence for an increased rate of cardiovascular events in patients with primary aldosteronism. J Am Coll Cardiol 2005;45:1243–1248.
6. Funder JW, Carey RM, Fardella C, et al. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an Endocrine Society clinical practice guideline. Endocrinol Metab 2008;93:3266–3281.
7. Melby JC, Spark RF, Dale SL, et al. Diagnosis and localization of aldosterone-producing adenomas by adrenal-vein catheterization. N Engl J Med 1967;277:1050–1056.
8. Stewart PM, Allolio B. Adrenal vein sampling for primary aldosteronism: time for a reality check. Clin Endocrinol 2010;72: 146–148.
9. Mulatero P, Bertello C, Sukor N, et al. Impact of different diagnostic criteria during adrenal vein sampling on reproducibility of subtype diagnosis in patients with primary aldosteronism. Hypertension 2010;55:667–673.
10. Magill SB, Raff H, Shaker JL, et al. Comparison of adrenal vein sampling and computed tomography in the differentiation of primary aldosteronism. J Clin Endocrinol Metab 2001;86: 1066–1071.
11. Phillips JL, Walther MM, Pezzullo JC, et al. Predictive value of preoperative tests in discriminating bilateral adrenal hyperplasia from an aldosterone-producing adenoma. J Clin Endocrinol Metab 2000;85:4526–4533.
12. Kempers MJ, Lenders JW, van Outheusden L, et al. Systematic review: diagnostic procedures to differentiate unilateral from bilateral adrenal abnormality in primary aldosteronism. Ann Intern Med 2009;151:329–337.
13. Zarnegar R, Bloom AI, Lee J, et al. Is adrenal venous sampling necessary in all patients with hyperaldosteronism before adrenalectomy? J Vasc Interv Radiol 2008;19:66–71.
14. Kline GA, Harvey A, Jones C, et al. Adrenal vein sampling may not be a gold-standard diagnostic test in primary aldosteronism: final diagnosis depends upon which interpretation rule is used. Int Urol Nephrol 2008;40:1035–1043.
15. Harvey A, Kline G, Pasieka JL. Adrenal venous sampling in primary hyperaldosteronism: Comparison of radiographic with biochemical success and the clinical decision-making with "less than ideal" testing. Surgery 2006;140:847–855.
16. Doppman JL, Gill JR Jr. Hyperaldosteronism: Sampling the adrenal veins. Radiology 1996;198:309–312.
17. Sawka AM, Young WF Jr, Thompson GB, et al. Primary aldosteronism: factors associated with normalization of blood pressure after surgery. Ann Intern Med 2001;135:258–261.
18. Zarnegar R, Young WF Jr, Lee J, et al. The aldosteronoma resolution score. Predicting complete resolution of hypertension after adrenalectomy for aldosteronoma. Ann Surg 2008;247: 511–518.