Primary Hyperaldosteronism

Effect of Adrenal Vein Sampling on Surgical Outcome

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Hypothesis: Adrenal vein sampling is superior to computed tomography for subtype differentiation of primary hyperaldosteronism.

Design: Retrospective review.

Setting: University medical center.

Patients: Forty-eight patients (32 men and 16 women) with biochemically confirmed primary hyperaldosteronism.

Main Outcome Measures: We compared demographic factors, results of biochemical and imaging studies (computed tomography and adrenal vein sampling), therapy, and patient outcomes.

Results: Mean ± SEM adrenal nodule size was 1.54 ± 0.2 cm. Adrenal vein sampling was performed in 41 (85%) of 48 patients, and it was successful in 39 (95%) of those 41 patients. Concordance between computed tomography and adrenal vein sampling was observed in 22 (54%) of the 41 patients. Thirty-two patients underwent successful laparoscopic adrenalectomy. There was 1 complication and no deaths. All 32 patients were cured of hypokalemia.

Conclusion: Adrenal vein sampling is superior to image-based techniques for subtype differentiation of primary hyperaldosteronism.

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P RIMARY HYPERALDOSTERONISM (PH) is a common cause of secondary hypertension, and recent evidence suggests that the prevalence of PH may be increasing.1-3 Although assays needed to establish the biochemical diagnosis have become routinely available, subtype differentiation is particularly challenging. Aldosterone-producing adenomas (APAs), bilateral hyperplasia (BH), primary unilateral hyperplasia, and familial hyperaldosteronism comprise the major subtypes, but APA and BH represent most cases of PH.4 Subtype differentiation is particularly important because surgical therapy for APA is curative, whereas the other subtypes are better managed with potassium-sparing diuretics or aldosterone receptor antagonists. Early studies5 suggested that the use of imaging studies to identify unilateral adrenal enlargement in patients with PH was sufficient to make this distinction. However, modern computed tomographic (CT) scanners detect incidental adrenal nodules (incidentalomas) in 0.35% to 5% of CT scans and contribute to the diagnostic dilemma.6-8 Many of these are nonfunctioning incidental nodules found at the time of evaluation for symptoms unrelated to adrenal origin.7-10

The diagnosis of APA and its localization in patients with PH can be attempted using a variety of techniques, including saline suppression, captopril stimulation, adrenal scintigraphy,6-8 [131I]iodomethyl-19-norcholesterol, and adrenal vein sampling (AVS). However, the accuracy of these techniques is variable, with the best results being those for AVS.11 Scintigraphy is of limited utility in PH because of the poor image resolution in nodules smaller than 1.5 cm,12 and most APAs are smaller than 15 mm.13,14 Enthusiasm for AVS has been dampened by the relative dearth of technical expertise required and the invasiveness of the technique. However, improved experience with interventional radiologic procedures and catheter-based vascular therapy has caused a resurgence of interest in AVS.

Few large studies15-17 have examined the accuracy of image-based diagnosis of APA using AVS. Some of these studies report an advantage of AVS over image-guided diagnosis; however, the variability in patient selection,15 limits on nodule size,16 and AVS technique (use of cor-
ticotropin and cutoff values for positive test results) limit conclusions. Furthermore, few of these studies focus on surgical therapy and outcomes of patients with APA.

We examined the utility of CT and AVS in all patients with biochemically confirmed PH seen at the affiliated hospitals and clinics of the University of Texas Southwestern Medical Center between February 1, 2001, and September 30, 2005. Specifically, we determined the accuracy of AVS compared with CT, examined the predictive value of AVS-derived biochemical ratios, and assessed the outcomes for surgically and nonsurgically managed patients.

We retrospectively reviewed the medical records of patients who underwent AVS for PH during a 4-year period (2000-2004). Demographic data, such as patient age, sex, and blood pressure (BP), were examined, as were the use of antihypertensive medications, potassium supplementation, results of biochemical and imaging studies (CT and AVS), and therapy. The biochemical diagnosis of PH was made by using plasma aldosterone concentration–plasma renin activity (PAC/PRA) screening test ratios and was confirmed by saline suppression. Screening test results were considered positive if there was a failure to suppress PAC in the presence of suppressed PRA, as described by other researchers. Patients with positive screening results underwent confirmation by measurement of 24-hour urinary aldosterone levels (>14.0 pg/24 h [>39 nmol/d]) after saline suppression.

ADRENAL CT

Most patients underwent abdominal CT at the University of Texas Southwestern Medical Center by a single radiologist (L.W.) using an Aquilion Super 4 (Toshiba Corp, Tokyo, Japan). Our protocol for adrenal CT is as follows. Scan mode is helical from the diaphragm through the middle of the kidneys. The patient undergoes initial noncontrast CT with 2×2-mm sections followed by injection of 100 mL of Omnipaque 300 (Sanofi Winthrop Markham, Ontario) at 3 mL/s using 2×2-mm sections with a 70-second delay and then 2×2-mm sections with a 10- to 15-minute delay.

ADRENAL VEIN SAMPLING

Adrenal vein sampling was performed by 4 interventional radiologists using the same technique, but 1 of these radiologists (B.D.) performed most of the AVS procedures. Our AVS protocol is as follows. When the patient arrives in the radiology suite, a peripheral venous blood sample is obtained for a baseline cortisol level, and corticotropin stimulation is commenced by administration of 0.25 mg of corticotropin (Cortrosyn; Amphastar Pharmaceuticals Inc, Rancho Cucamonga, Calif) in 300 mL of 3% dextrose in water at a rate of 100 mL/h for the duration of the procedure. This infusion is started at least 20 minutes before obtaining samples.

Bilateral 5F sheaths are inserted into the common femoral veins. Through 1 of these sheaths, a Simmons-2 catheter with 2 small side holes is placed in the left renal vein. Then, a search for the right adrenal vein is performed using 5F catheters. Catheterization is confirmed by venography. A 10-mL blood sample is slowly obtained from the right adrenal vein. Immediately thereafter, the left renal vein catheter is repositioned into the left adrenal vein and confirmed by venography before slowly withdrawing a 10-mL blood sample. Once adrenal vein specimens are obtained, either the left- or right-sided catheter is repositioned into the inferior vena cava (IVC) for a 10-mL IVC blood sample, and finally, both catheters are removed, and a 10-mL peripheral venous sample is obtained from 1 of the sheaths. Aldosterone and cortisol levels are measured by radioimmunoassay.

We consider adrenal vein cannulation to be successful when the cortisol levels in both adrenal veins are 3 times (or more) higher than the cortisol level in the IVA, whereas lateralization is considered positive when the adrenal vein aldosterone-cortisol (A/C) ratio in the dominant side is 4 times greater than the A/C ratio in the contralateral side.

STATISTICAL ANALYSIS

Results are expressed as mean ± SEM. Comparisons between 2 groups were performed using the t test and among multiple groups using analysis of variance with post hoc analysis. We also compared the sensitivity and specificity of adrenal vein A/C ratios and the A/C ratio of the higher (dominant) vs lower (non-dominant) adrenal glands at various thresholds.

PATIENT CHARACTERISTICS AND PREOPERATIVE FACTORS

Forty-eight patients (32 men and 16 women) had biochemically confirmed PH. Forty-one patients (85%) underwent AVS for PH during the 56 months between February 1, 2001, and September 30, 2005. Mean patient age was 52 ± 2 years. All the patients were hypertensive and being treated with an average of 3 antihypertensive medications. Their mean BP was 157/96 mm Hg. Furthermore, 79% of the patients required potassium supplementation for hypokalemia (mean serum potassium level, 3.5 ± 1 mEq/L). The mean PAC was 52.4 ± 15 ng/dL (1.4 ± 0.4 nmol/L), and the mean PRA was 1.26 ± 0.3 pg/mL (0.03 ± 0.007 pmol/L) per hour. The mean aldosterone-renin ratio was 167 ± 61. Patients with APAs had higher serum aldosterone levels and PRA than patients with bilateral aldosterone hypersecretion (38.0 vs 22.0 ng/dL [1.6 vs 0.6 nmol/L] and 1.36 vs 0.7 pg/mL [0.032 vs 0.016 pmol/L], respectively).

ADRENAL GLAND CT

Interpretable CT reports were available for 47 patients and revealed 10 right-sided abnormalities, 18 left-sided abnormalities, 14 bilateral abnormalities, and 5 normal adrenal glands. The mean size of the adrenal nodules in this study was 1.5 ± 0.2 cm.

ADRENAL VEIN SAMPLING

Adrenal vein sampling was performed in 41 (85%) of 48 patients. Bilateral adrenal vein cannulation was successful in 39 (95%) of the 41 patients. The right adrenal vein was not cannulated initially in 6 patients but was successfully accessed in 4 patients who underwent another AVS procedure. Procedure-related adrenal hemorrhage occurred in 1 patient, and it resolved spontaneously, with no apparent adverse outcome. Overall, the mean adrenal vein–IVA A/C ratio was 20. The mean right adrenal
vein A/C ratio was 30 in patients with right-sided hypersecretion, and the mean left adrenal vein ratio was 14 in patients with left-sided hypersecretion.

Using the criteria mentioned previously herein (adrenal vein A/C ratio in the dominant side is 4 times greater than that in the contralateral side), unilateral aldosterone hypersecretion was identified in 29 (71%) of 41 patients. Fourteen patients lateralized to the right adrenal gland, and 15 lateralized to the left adrenal gland. Twelve patients had bilateral adrenal hyperaldosteronism. The A/C ratio in the unilateral hypersecreting adrenal gland was 34 times the ratio in the contralateral side. The mean dominant-nondominant A/C ratio in patients with BH was 1.9.

AVS RATIOS

We examined the predictive value of 3 biochemical ratios (adrenal vein A/C ratio, dominant-nondominant A/C ratio, and contralateral adrenal vein–IVA A/C ratio) for predicting the presence of unilateral aldosterone hypersecretion. The adrenal vein A/C ratio greater than 4 had the best predictive value. The mean dominant-nondominant A/C ratio was higher in patients who underwent surgery, but this difference did not achieve statistical significance (Figure 1).

PREDICTIVE VALUE OF CT VS AVS

Forty patients underwent both CT and AVS. The side of abnormality seen on CTs was compared with AVS results to determine concordance between the 2 studies. Overall, 22 (55%) of 40 patients had concordance between CT and AVS. Twenty patients had unilateral CT abnormalities, and 14 (70%) of them lateralized to the same side (concordant). Of the remaining 6 patients with unilateral CT abnormalities (3 left and 3 right), 1 patient each lateralized to the opposite side and 2 patients each had bilateral hypersecretion. Only 5 of 15 patients (33%) with bilateral CT abnormalities showed concordant bilateral aldosterone hypersecretion. The other 10 patients (67%) demonstrated unilateral hypersecretion. Of the 5 patients with normal-apparing adrenal glands on CT, 1 patient each lateralized to 1 side, and the other 3 patients had bilateral hypersecretion. We found no significant difference between the CT/AVS concordance in patients with micronodules (<1 cm, 67% concordance) and macronodules (>1 cm, 60% concordance). However, the mean age of patients with bilateral CT abnormalities was significantly higher than that of patients with unilateral abnormalities (58±14 vs 47±10 years; \( P = .008 \)).

Patients with BH diagnosed by AVS were compared with those with a unilateral APA. There was no significant difference in mean age (51.0 vs 51.7 years) or malefemale ratio (2:1) between patients with BH and APA. However, the mean PAC/PRA ratio for those with BH vs APA was 50 vs 196.

THERAPY AND OUTCOME

Adrenalectomy

Thirty-two patients (21 men and 11 women; 14 right adenomas and 18 left adenomas) underwent laparoscopic adrenalectomy for PH: 25 underwent AVS and localized to 1 side for excess aldosterone production and 7 underwent adrenalectomy without previous AVS. Mean operative time was 102±55 minutes, and the mean hospital stay was 1.7±1 days. Mean estimated blood loss was 46±34 mL. All but 1 of the 32 patients were cured of hypokalemia (none required potassium supplements), 6 patients (19%) completely stopped using antihypertensive medication, whereas an additional 15 patients (47%) were normotensive (systolic BP <140 mm Hg) when taking a reduced dosage of antihypertensive medication. Compared with preoperative BPs, the mean postoperative BPs were significantly lower in surgical patients (157/96 vs 127/79 mm Hg; \( P = .007 \)). Patients were taking an average of 1.8 antihypertensive medications after surgery compared with 3 medications before surgery. The mean potassium level was 4.3 mEq/L after surgery and 3.5 mEq/L before surgery. One patient developed a postoperative deep vein thrombosis that resolved without sequelae after anticoagulation therapy. There were no intraoperative complications, conversions to open adrenalectomy, or perioperative deaths. Pathological examination findings revealed 13 adrenal adenomas that averaged 1.32 cm. Of the 2 patients with normal-apparing adrenal glands on CT who underwent adrenalectomy, 1 had a 0.9-cm cortical adenoma and the other had cortical nodular hyperplasia. Both patients had resolution of hypokalemia after surgery.

We compared 25 patients who underwent AVS before adrenalectomy with 7 patients who underwent adrenalectomy without AVS. In the former cohort, 4 patients stopped taking all antihypertensive medications (16%), and 2 (29%) of the 7 patients without AVS were cured of hypertension. Six of these 7 patients were cured of hypokalemia. These patients all had unilateral nodules seen on CT. The mean size of these nodules was 1.9 cm (vs 1.5 cm in the AVS group). One of these 7 patients did not improve after surgery. This patient experienced recurrent hypertension (BP, 194/120 mm Hg) and

Figure 1. Box plots illustrating the dominant-nondominant aldosterone-cortisol ratios in patients who underwent surgery vs patients who were managed medically. The boundary of the box closest to zero indicates the 25th percentile, the line within the box marks the median, and the boundary of the box farthest from zero indicates the 75th percentile. Whiskers above and below the box indicate the 90th and 10th percentiles. Solid circles are outliers.
hypokalemia several months after a laparoscopic adrenalectomy consistent with a wrong diagnosis of APA. This patient’s CT initially demonstrated a 0.8-cm cortical nodule in the right adrenal gland, and she had an elevated PAC/PRA ratio of 55.6. Her hypertension is currently controlled with 3 antihypertensive drugs and potassium supplementation. Another patient in the non-AVS group required an increased dosage of antihypertensive medication after surgery. The mean preoperative serum potassium level was 3.4 mEq/L in the AVS group and 2.7 mEq/L in the non-AVS group.

**Medical Therapy**

Fifteen patients (12 with BH and 3 with APA) were treated medically (8 with spironolactone and 4 with eplerenone) because of AVS-diagnosed BH or refusal of surgery. Hypertension improved in 8 of these patients, whereas 2 patients developed worsening hypertension. There were no significant differences between the surgical and nonsurgical groups (Table).

Based on these findings, a CT-based approach to the evaluation of patients with PH would have led to inappropriate therapy in 45% of the patients. Specifically, 12 (60%) of 20 patients would have been incorrectly excluded from having surgery, whereas noninvasive surgery or wrong side surgery would have been performed in 6 (30%) of 20 patients (Figure 2).

**COMMENT**

This study demonstrates that AVS is markedly superior to abdominal CT in localizing APAs in patients with PH. Successful bilateral adrenal vein cannulation is feasible, and the procedure is associated with low morbidity. The sole use of image-based methods for diagnosing APA or BH would have resulted in inappropriate or suboptimal treatment in almost half of the patients in this study.

These findings are similar to those of previous studies, which confirm an important role for AVS in patients with PH. Rossi and colleagues found AVS to be highly diagnostic of APA in patients with equivocal CT or magnetic resonance imaging results. Although their results remain important, patients with “unequivocal” imaging studies were excluded, as were those with tumors larger than 1.8 cm. Outcomes in patients who underwent surgery are also lacking in their study. We believe that the inclusion of all patients with PH in the present study provides information that is easier to extrapolate to all patients with biochemically confirmed PH, regardless of CT findings. Young and associates imposed no CT-based restriction criteria in their study of 203 patients with PH, 92 of whom underwent adrenalectomy. They also noted a high rate of bilateral adrenal cannulation (95%) despite the relatively more stringent criteria used to document successful adrenal vein cannulation (>5 times the IVC cortisol level). They concluded that using CT alone would have led to unnecessary surgery in 24% of the patients and that another 22% of the patients would have been denied surgery inappropriately. We found similar discordant findings between CT and AVS in 30% of the patients with unilateral adrenal abnormalities and in 67% of those with bilateral abnormalities. The former group is of particular concern because of the potential for removal of the biochemically normal adrenal gland. We found no relationship between patient age and the prevalence of micronodules, perhaps because of the smaller sample size; however, the average age of patients with bilateral adrenal lesions was significantly higher than that of those with unilateral lesions, supporting the premise that older patients have a tendency to develop incidental adrenal abnormalities.

Adrenal vein sampling is accurate for predicting the side of aldosterone hypersecretion in APA, and it confirms BH; however, the biochemical ratio with the best predictive value is unclear. Adrenal vein aldosterone levels are unreliable; therefore, most studies suggest the use of A/C ratios, sometimes referred to as the *corrected aldosterone*. This ratio is necessary to account for fluctuations in aldosterone secretion due to the invasive procedure and to correct for “dilution” of the adrenal vein sample with blood aspirated from the IVC or left renal vein. However, whether one should use the raw cor-

### Table. Comparison Between Surgical Patients and Medically Managed Patients

<table>
<thead>
<tr>
<th></th>
<th>Surgical Patients</th>
<th>Nonsurgical Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SEM, y</td>
<td>52.0 ± 12.0</td>
<td>51.5 ± 15.0</td>
</tr>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
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<tr>
<td>M</td>
<td>21</td>
<td>10.5</td>
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<tr>
<td>F</td>
<td></td>
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<tr>
<td>Nodule size, mean ± SEM, cm</td>
<td>1.7 ± 0.5</td>
<td>1.5 ± 0.4</td>
</tr>
<tr>
<td>Serum aldosterone, mean ± SEM, ng/mL</td>
<td>58 ± 104</td>
<td>21 ± 10</td>
</tr>
<tr>
<td>PAC/PRA ratio, mean ± SEM</td>
<td>196 ± 373</td>
<td>51 ± 58</td>
</tr>
<tr>
<td>Peripheral vein A/C ratio, mean ± SEM</td>
<td>44 ± 113</td>
<td>8 ± 12</td>
</tr>
</tbody>
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Abbreviations: A/C, aldosterone-cortisol; PAC/PRA, plasma aldosterone concentration–plasma renin activity.

SI conversion factor: To convert serum aldosterone to nanomoles per liter, multiply by 0.0277.

![Figure 2](https://example.com/figure2.png)

Figure 2. Projected effects of computed tomography (CT)–guided therapy. BH indicates bilateral hyperplasia; PH, primary hyperaldosteronism; and Tx, treatment.
rected aldosterone from the suspected adrenal gland, the A/C ratio of dominant-nondominant aldosterone, or the suppressed aldosterone from the contralateral adrenal gland is still debated.

Doppman et al\textsuperscript{18,21} found that after corticotropin infusion, most patients with APA or primary adrenal hyperplasia demonstrated a corrected aldosterone (A/C ratio) greater than 5:1 between the dominant and nondominant sides. However, more recently, Rossi et al\textsuperscript{10} found that the ratio of corrected aldosterone in the dominant compared with the nondominant adrenal gland provided the best sensitivity, and the threshold of greater than 2 had the best combination of sensitivity and false-positive rates. We noted a similar trend in the present study. The adrenal vein corrected aldosterone–IVC and the dominant-nondominant ratios performed well (at a threshold of >3 or 4) in predicting APA during this study. At these thresholds, both studies demonstrated high sensitivity and specificity. As expected, increasing the threshold beyond 4 reduced the sensitivity. Using these criteria, AVS and CT findings correlated in 22 of 41 patients, for a concordance rate of 54%. In those with APA, the concordance rate was 70%. This is similar to the 51% to 65% concordance rate in patients with APA described by Young et al.\textsuperscript{15} We identified a much lower concordance rate (33%) for patients with bilateral CT abnormalities. Specifically, two thirds of this group demonstrated unilateral hypersecretion, underscoring the importance of AVS in patients with any bilateral abnormalities. Finally, we noted a 60% concordance rate in 5 patients with normal findings on adrenal CT, that is, bilateral hypersecretion. This is similar to findings by Young et al,\textsuperscript{15} who noted a 41% unilateral hypersecretion rate in patients with normal findings on adrenal CT.

Laparoscopic adrenalectomy was associated with low morbidity rates and a short hospital stay in the present study. As with other studies,\textsuperscript{22,23} hypokalemia resolved in all the patients who underwent adrenalectomy; however, the effect of adrenalectomy on hypertension was variable.\textsuperscript{23,24} Although the mean postoperative BPs were significantly lower than the mean preoperative levels and the average number of antihypertensive drugs used was lower, individual responses varied. This is similar to findings by others and probably reflects the underlying prevalence of essential hypertension in these patients and the development of fixed hypertension in patients with a secondary cause. However, recent evidence suggests significant cardiovascular benefit by reducing circulating aldosterone levels despite persistent hypertension.\textsuperscript{25-30} Therefore, we believe that the advantage of reducing aldosterone levels in these patients goes beyond resolution of hypokalemia and hypertension.

A group of 7 highly selected patients seen early in our experience had good outcomes despite not undergoing AVS for localization. These patients had larger nodules and more severe hypokalemia, but 2 of them developed worsening hypertension. We would consider offering unilateral adrenalectomy to patients with large unilateral nodules and completely normal contralateral adrenal glands in the presence of severe PH.

This study did not address the additional cost of AVS, a factor that should be considered in evaluating the approach to therapy. The recent availability of a selective aldosterone receptor antagonist, eplerenone, provides a safe and effective means of preventing the deleterious effects of excess circulating aldosterone. As the cost of such drugs decreases, and the safety profile improves, enthusiasm to treat patients with APA with these agents may ensue. In fact, studies\textsuperscript{31,32} have documented improvement in BP, and hypokalemia in patients with APA managed medically using aldosterone receptor antagonists. Although many researchers believe that the cost-benefit analysis favors adrenalectomy in patients who can withstand surgery, few direct comparisons exist. Sywak and Pasieka\textsuperscript{33} suggested a cost-benefit advantage for adrenalectomy compared with life-long medical therapy in patients with PH; however, that study was underpowered.

The age of the patient, the severity of hypertension, and comorbidity must be considered in the therapeutic decision for individual patients. The lack of long-term surveillance of patients in this study is a limitation because the beneficial effects of therapy could occur long after surgery. However, we have used the resolution of hypokalemia as a surrogate for relief of hyperaldosteronism, understanding full well that we may have patients with persistent or recurrent hyperaldosteronism long after unilateral adrenalectomy, hence our ongoing follow-up of these patients.

Abdominal CT is unreliable in correctly identifying the abnormal adrenal gland in patients with PH due to APAs, particularly when both adrenal glands are abnormal. We believe that the liberal use of adjunctive diagnostic studies, such as AVS, is crucial for accurate subtype differentiation in patients with PH. Adrenal vein sampling is accurate and has a low morbidity rate. Laparoscopic adrenalectomy is associated with excellent outcomes in patients with APAs.

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\textbf{REFERENCES}

5. White EA, Schambelan M, Rost CR, Biglieri EG, Moss AA, Korobkin M. Use of

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a study I think by Dr Pasieka and colleagues from several years ago which examines the medical management with spirono-
lactone vs surgery, and they demonstrated cost benefit for sur-
gical patients who underwent adrenalectomy. This question
probably needs to be examined in the future.

Clive S. Grant, MD, Rochester, Minn: We agree entirely
that AVS is an excellent and vitally important technique, but
not necessarily for every patient. Have you found a subgroup
of patients for whom you might be able to rely on CT, for ex-
ample, a younger patient with more severe disease, with a single
nodule in 1 adrenal gland and the contralateral adrenal that is
well visualized and normal? Second, if guided by AVS, how often
have you identified unilateral hyperplasia as the pathology
after adrenalectomy, and what has been the outcome of those
patients?

Dr Nwariaku: The findings with AVS are similar to those
presented by your group. Currently, we offer AVS to all our
patients. Part of the reason is that we see patients with abdomi-
nal CT obtained from outside radiologists, and many of these
are either inadequately performed or improperly interpreted.
So we are either repeating them or sending them to AVS.

The subgroup of patients that I would anticipate would not
require AVS would be patients such as those I just described,
the patient with more severe hyperaldosteronism, more se-
vere hypokalemia, and larger nodules. And if you examine the
older data, when CT was used and found to be accurate, those
nodules were usually 2 and 2.5 cm, and the other adrenal gland
was normal. So such patients may benefit from adrenalectomy
without AVS.

Quan-Yang Duh, MD, San Francisco, Calif: Of the 20 pa-
tients who had unilateral disease by CT scan, 14 had a concor-
dant study and 6 had a discordant study. Were there any dif-
ferences in the size of the tumors in the concordant vs the
discordant ones? We all agree that if the CT scan shows bilat-
eral normal or bilateral abnormal glands, you need venous sam-
pling. But the discordant percentage of 30% seems high.

The second question is, after a positive venous sampling find-
ing high secretion on one side only, have you ever had a failed
operation? We have at least 1 failure after a positive venous sam-
pling. You would expect selected venous catheterization to be
100% accurate, if positive, but it is not.

Dr Nwariaku: There were no differences in the sizes of the
nodules in the discordant or discordant lesions. Part of that
may just be that this subgroup is a highly selected group and
has really small tumors, so I am not sure that we would find
those differences.

Now, regarding the question of failed AVS, this is a small group
of patients, but we haven’t had that problem. Now, the Mayo Clinic
reports about a 1% incidence of primary unilateral adrenal hy-
perplasia. Obviously, the long-term follow-up is where the an-
swer to that question will lie. It is possible that there are patients
who have bilateral hyperaldosteronism which starts off on one
side and eventually develop hypersecretion on the other side, or
this could be pure primary unilateral hyperplasia.

Samuel Snyder, MD, Temple, Tex: Here is not an uncom-
mon clinical problem that we might face. Adrenal vein sam-
ping (as you pointed out) of the right adrenal vein is difficult
to sometimes access, but we get results from the left adrenal
vein in the patient with bilateral adrenal nodules. The left ad-
renal vein aldosterone is increased, but we have no values from
the right. How do you manage that patient?

Dr Nwariaku: I think there are 2 patients in this series where
we had that problem. And we cheated a little bit. If we can dem-
strate that the samples from the area of the right adrenal vein,
even if we are not absolutely sure of right vein cannulation, are
suppressed compared with the IVC samples, and if the ratio is
high, that is, 10:1, for instance, instead of 4:1, we have con-
sidered that successful and operated on those 2 patients and
they did just well. So that is one possibility. The other way would
be to put the patient on eplerenone. Another option is to re-
peat the AVS procedure. As I showed, 2 patients required a re-
peat sampling study to obtain the correct numbers.

Cord Sturgeon, MD, Chicago, Ill: My comments are di-
rected toward the data in your abstract. You stated in the ab-
stract that 20 patients had undergone successful adrenalecto-
tomy. By looking at the data, I assume that this group of 20 is
composed of 12 patients with unilateral CT scan findings and
discordant lateralization with AVS and 8 patients with bilat-
eral nodules which then lateralized on AVS, making the 20.

What about those 5 or 6 patients who had a unilateral nod-
ule on the CT scan but discordant lateralization by AVS? Since
we know that aldosteronomas are almost always very small,
0.5 to maybe 2 cm, and in many cases they are smaller than the
limit of resolution of the imaging studies that are used, shouldn’t
we be resecting all of those adrenal glands that lateralized to even
the normal-appearing side? What did you do in those cases?

Dr Nwariaku: My short answer would be, yes, if they have
biochemically confirmed PH using fairly stringent criteria, then
they have the disease. And if the lesion is not visible on CT scan
but the adrenal venous sampling studies are clear, we would
perform adrenalectomy on the localized side.

Dr Sturgeon: But nevertheless, if you had a nodule on one
side and your AVS showed the secretion was contralateral, you
would take out the normal-looking adrenal gland?

Dr Nwariaku: Yes, we would resect the normal-appearing
gland.

Thomas Biehl, MD, Seattle, Wash: I know it wasn’t part of
your study, but I am curious to know if the norcholesterol ana-
logue nuclear medicine study NP-59 [6-β-(131I)iodomethyl19-norcholesterol] has been useful at all in your institution and
in what setting.

Dr Nwariaku: We have not used the norcholesterol or
NP-59. Actually, I don’t think that this disease is one where it
has much benefit, the reason being that about 20% of patients
with PH have tumors that are usually less than 1.5 cm, which
is below the limits of resolution for NP-59 scintigraphy. So we
haven’t used it. In addition to that, it is a 3- to 5-day test and
you have to obtain the isotope from outside institutions.