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Contralateral adrenal abnormalities in Conn's syndrome

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ABSTRACT

Background: During the course of evaluation for primary hyperaldosteronism, cross-sectional imaging is obtained in efforts to identify patients with an aldosterone producing adenoma (APA). A subset of these patients will have a synchronous, contralateral adrenal abnormality. Adrenal vein sampling (AVS) further guides clinical decision making by identifying unilateral (APA) *versus* bilateral hypersecretion. In the subset of patients with contralateral adrenal abnormalities, it is unclear how this affects the durability of an adrenalectomy for APA. This study characterizes this group of patients to assess the efficacy of surgical intervention.

Methods: A retrospective review of patients undergoing adrenalectomy for APA based on AVS at a university practice. Preoperative and postoperative patient characteristics, laboratory evaluations, imaging results, and final pathology were noted.

Results: From 2000 to 2011, 103 patients with APA underwent unilateral adrenalectomy. Eighteen patients (17%) had discordant results between AVS and imaging. Most of these patients were male (78%), and the mean age was 57 ± 13 y. Median duration of follow-up was 3.5 y [1 y, 6 y]. All patients with initial hypokalemia were rendered normokalemic after the operation. Four patients increased their antihypertensive regimen during the follow-up period. These patients all had nodular hyperplasia on final pathology.

Conclusions: In patients with bilateral adrenal abnormalities who have undergone unilateral adrenalectomy for primary hyperaldosteronism, patients with clear APAs on final pathology appear to have durable outcomes after resection. Conversely, nodular hyperplasia on final pathology may be a risk factor for ongoing aldosterone hypersecretion. An algorithm for biochemical surveillance in this subset of patients should be considered.

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1. Introduction

Primary hyperaldosteronism (PH) is a group of disorders caused by an autonomous overproduction of aldosterone that results in hypertension and hypokalemia. Once thought to be a rare cause of hypertension, it is now recognized as the most common form of secondary hypertension [1,2]. It is accountable for 5%–12% of all hypertensive patients when applying aldosterone-to-renin ratios as a screening test among both hypokalemic and normokalemic hypertensive subjects [3].

Distinction between the two main subtypes of PH (aldosterone producing adenoma [APA] and idiopathic

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hyperaldosteronism) is essential to guide therapy. APAs are treated surgically, whereas idiopathic hyperaldosteronism involves both adrenal glands and is medically managed. Subtype differentiation is usually based on cross-sectional imaging in conjunction with more invasive testing via adrenal vein sampling (AVS). Several studies have demonstrated the superiority of AVS over CT scans in lateralizing the functional adenoma, reporting discordance rates of up to 45% between the two modalities [4–7]. In addition, CT scans are notoriously unreliable for detecting microadenomas, detecting <25% of adenomas that were <1 cm [8]. Thus, AVS remains the gold standard for localizing APAs in PH.

Given the relatively high rate of discordance between imaging and AVS, there is a subset of patients who have undergone adrenalectomy for an APA who have a synchronous, contralateral adrenal abnormality. Four case reports to date have described patients with a unilateral secreting aldosteronoma in the setting of bilateral adrenal abnormalities on imaging [9–12]. In these patients, AVS plays a critical role in aiding the clinician to lateralize the hyperfunctioning gland. However, it is unclear in this subset of patients how the presence of a contralateral adrenal abnormality affects the durability of adrenalectomy for APA. This study characterizes this subset of patients and assesses the efficacy of surgical intervention.

2. Methods

After institutional review board approval, a retrospective review of patients with APA who underwent unilateral adrenalectomy by an endocrine surgery group at a large urban academic medical center between March 2000 and March 2011 was performed. All patients underwent a biochemical workup to rule out other sources of functional adrenal tumors and to confirm the diagnosis of primary aldosteronism. Screening criteria for primary aldosteronism included aldosterone level >15 ng/dL with a suppressed renin or aldosterone-to-renin ratio >20. Patients who did not meet screening criteria but were still suspected of having primary aldosteronism underwent a subsequent salt suppression test to confirm the diagnosis [13]. Confirmatory testing was used at the discretion of the surgeon and/or endocrinologist, in cases where the biochemical diagnosis for hyperaldosteronism was not clear.

Cross-sectional imaging (CT scan or MRI) and AVS were used for lateralization of the aldosteronoma for each patient. AVS was performed by four interventional radiologists per protocol [14]. Simultaneous specimens (aldosterone and cortisol levels) were collected under cosyntropin stimulation. Blood samples were obtained from the inferior vena cava, peripheral vein, right adrenal vein, and left adrenal vein. Adrenal vein cannulation was considered successful when the cortisol levels in both adrenal veins were at least three times higher than the cortisol level in the inferior vena cava [5]. Lateralization was determined based on the ratio of aldosterone to cortisol from each gland, as previously described [14].

Only those patients with discordant results between AVS and radiologic imaging were included in the study. Discordant results occurred in two scenarios: (1) imaging revealing a unilateral adrenal abnormality with AVS lateralizing the functional adenoma to the contralateral adrenal gland or (2) imaging revealing bilateral adrenal abnormalities with AVS lateralizing to a single gland. In instances where there was discordance between the imaging and AVS results, the AVS results guided surgical decision making. Patients who did not have both preoperative imaging and AVS available, as well as those with concordant results, and those with no radiologic abnormality were excluded from the final sample.

Descriptive statistics were used to evaluate postoperative blood pressure, potassium levels, plasma aldosterone and renin concentrations, aldosterone-to-renin ratios, and imaging of the remaining adrenal gland. Postoperative blood pressure was obtained during a postoperative clinic appointment. Medians with interquartile ranges or mean ± standard deviation are reported where appropriate, unless otherwise specified. For the subjects who had bilateral nodules, the mean nodule size of the abnormality was compared to the mean nodule size of the functional tumor using a student *t*-test (GraphPad Prism 5; GraphPad Software, La Jolla, CA), with $P < 0.05$ indicating significance.

3. Results

One hundred three subjects underwent unilateral adrenalectomy for APA based on AVS results between March 2000 and March 2011. Eighteen (17%) had discordant results between AVS and radiologic imaging and made up the study population. Most of these patients were male (78%), and the mean age was 57 ± 13 y.

The median preoperative aldosterone-to-renin ratio was 39.6 [17.6, 60], with a median aldosterone of 28 ng/dL [16.5, 37.3] and a median renin of 0.6 ng/mL [0.6, 1.1] (Table 1). Two-thirds of subjects had completely suppressed renin levels preoperatively. The remaining four subjects had preoperative renin levels ranging from 1.1 ng/mL to 2 ng/mL.

All adrenalectomies were performed in the minimally invasive fashion: 17 via laparoscopic transabdominal approach and one via retroperitoneoscopic approach. The median hospital stay was 1 d with a maximum stay of 2 d, and there were no recorded complications. Six patients were lost to follow-up postoperatively.

Table 1 – Study cohort demographics and clinical characteristics.

Mean age (y)	57 ± 13
Gender	
Male	14
Female	4
Number of antihypertensive medications	3 ± 1
Potassium (reference range, 3.6–5 mmol/L)	3.1 ± 0.4
Median aldosterone (reference range ≤ 21 ng/dL)	28 [16.5, 37.3]
Median renin (reference range ≤ 0.6–4.3 ng/mL)	0.6 [0.6, 1.1]
Median aldosterone/renin ratio	39.6 [17.6, 60]
Largest diameter of functional nodule on imaging (cm)	1.7 ± 0.8