

Long-term blood pressure control in patients undergoing adrenalectomy for primary hyperaldosteronism

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Background. Data on long-term blood pressure (BP) control after adrenalectomy for primary hyperaldosteronism are limited. We analyzed long-term outcomes to identify factors predictive of cure.

Methods. We performed a retrospective cohort study of patients undergoing adrenalectomy for primary hyperaldosteronism (1997–2013). BP and antihypertensive medications were assessed at long-term follow-up (≥ 12 months). Primary outcome was cure, defined as normotension off antihypertensives.

Results. Of 85 patients, 15.3% ($n = 13$) were cured, 54.1% ($n = 46$) were normotensive while remaining on anti-hypertensives, and 30.6% ($n = 26$) were hypertensive. Younger age ($P = .011$), female sex ($P < .001$), lesser body mass index ($P = .018$), shorter duration of hypertension ($P = .002$), lower creatinine ($P = .001$), and fewer preoperative antihypertensive medications ($P < .001$) were associated with cure. Female sex, body mass index ≤ 25 kg/m², hypertension < 5 years, creatinine ≤ 0.8 mg/dL, and < 2 antihypertensives were incorporated into a scoring system. For a score of 0–1 ($n = 61$) the cure rate was 3%; 100% of patients with a score of 4–5 ($n = 3$) were cured. This scoring system performed comparably to the Aldosterone Resolution Score, which has been used to evaluate short-term postoperative outcomes.

Conclusion. This is the largest study to identify factors associated with long-term BP control after adrenalectomy and incorporate these into a scoring system. These data provide a potential tool to guide preoperative patient counseling. (*Surgery* 2014;156:1394-403.)

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PRIMARY HYPERALDOSTERONISM is one of the few potentially curable causes of hypertension. Previously thought to be rare, it has now been identified in approximately 11–20% of patients with hypertension resistant to medical management.^{1,2} The long-term sequelae of untreated hypertension have been documented extensively and include potentially irreversible cardiovascular and renal damage. Multiple studies suggest that target organ damage is more extensive,^{3–5} and cardiovascular events more common,^{6,7} in the setting of hypertension secondary to primary hyperaldosteronism. Indeed, primary hyperaldosteronism has been shown to cause target organ dysfunction independent of hypertension.⁸ Early detection and

appropriate treatment of primary hyperaldosteronism is therefore of paramount importance in preventing long-term morbidity and mortality.

Idiopathic bilateral adrenal hyperplasia is the most common cause of primary hyperaldosteronism; aldosterone-producing adenoma is the second most frequent, accounting for approximately 35% of cases.⁹ Other less-common causes include unilateral adrenal hyperplasia, aldosterone-secreting adrenocortical carcinoma, glucocorticoid-remediable hyperaldosteronism, and ectopic aldosterone secreting tumors. Whereas bilateral hyperplasia is best managed medically, ipsilateral adrenalectomy is the standard of care for unilateral oversecretion of aldosterone caused by aldosterone-producing adenoma and unilateral hyperplasia.

Despite the potentially curable nature of primary hyperaldosteronism caused by aldosterone-producing adenoma and unilateral hyperplasia, only approximately one-third of patients experience complete normalization of blood pressure off all antihypertensive medications after surgery^{10,11}; the remainder benefit from operative intervention,

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experiencing improved blood pressure control or requiring fewer antihypertensive medications. Resolution of hypertension typically is evaluated 6–12 months after surgery, and numerous studies have identified factors associated with short-term outcomes after adrenalectomy for primary hyperaldosteronism^{11–13}; however, data on long-term blood pressure control is limited. In this study, we evaluated long-term outcomes in our large series of patients undergoing adrenalectomy for primary hyperaldosteronism.

METHODS

We performed a retrospective cohort study of all patients undergoing adrenalectomy for primary hyperaldosteronism due to aldosterone-producing adenoma or unilateral hyperplasia at a tertiary medical center during a 16-year period (1997–2013). Consecutive patients were identified in our prospectively maintained endocrine surgery registry. Children (<18 years of age) were excluded.

Data abstracted included patient demographics, biochemical testing, antihypertensive medications, and blood pressure measurements. Patients were referred routinely for adrenal vein sampling. Comorbid renal disease was defined as chronic renal insufficiency, chronic renal failure, or any known renal disease, which in this cohort included renal artery stenosis, fibromuscular dysplasia, nephrolithiasis, and polycystic kidney disease.

Standard blood pressure criteria were used, with hypertension defined as $\geq 140/90$ mm Hg. Postoperative follow-up data were obtained at the patient's clinic visit 2–3 weeks after operation. Short-term follow-up was defined as 6–12 months after surgery. Long-term follow-up was defined as ≥ 12 months after surgery. Of 164 patients who underwent surgery, 68.3% ($n = 112$) did not have follow-up data in the medical record and were contacted by telephone to obtain current blood pressure measurements and antihypertensive medication regimens. Patients who were unable to be reached or who did not have recent or exact blood pressure measurements were excluded from the study. Long-term follow-up data were obtained for a total of 85 patients (52%) who constituted the study population. Of the study population, 61% ($n = 52$) had data in the medical record, whereas 39% ($n = 33$) had data obtained by telephone follow-up. Of the study population, 31 patients (37%) also had complete short-term follow-up data available in the medical record.

Primary outcome was cure, defined as normotension off antihypertensive medications. Group comparisons were made using the Student *t* test, χ^2

test, or Wilcoxon rank sum test, as appropriate. To dichotomize continuous variables, receiver operating characteristic (ROC) curves were generated, and values with maximal sensitivity were identified. For ease of use, values were rounded to the nearest integer or clinically appropriate value. The 5 factors associated with cure were incorporated into an unweighted scoring system in which 1 point was assigned per risk factor, for a possible score range of 0–5 points.

The Aldosternoma Resolution Score (ARS) as described by Zarnegar et al,¹³ is a 4-item, weighted scoring system (possible score range of 0–5 points), which was developed and validated on primary hyperaldosteronism patients 6 months after adrenalectomy. To determine whether the ARS performed well in long-term follow-up, we validated it in our cohort in accordance with published data, and compared it to our own scoring system using ROC curves and 95% confidence intervals (CIs).

Institutional review board approval for this study was obtained from the University of Pennsylvania. Statistical analysis was performed using STATA/IC 12.1 software (Stata Corporation, College Station, TX).

RESULTS

Cohort characteristics. Of 164 patients identified for inclusion, long-term follow-up data were obtained for 85 patients (51.8%), who were included in the final analysis. Mean age was 51.5 ± 10.9 years; 37.8% of patients were female ($n = 62$; Table 1). The majority of patients were white (65.9%, $n = 108$), with black as the second most common ethnicity (23.2%, $n = 38$). The median duration of preoperative hypertension was 10 years (interquartile range 4–20 years). On preoperative evaluation, patients were on a mean of 3.5 ± 1.5 antihypertensive medications, with a mean systolic blood pressure (SBP) of 152.5 ± 21.1 mm Hg. On postoperative follow-up 2–3 weeks after surgery, patients were on a decreased number of antihypertensive medications (1.8 ± 1.5) with an improved a mean SBP of 136.2 ± 16.8 mm Hg. At long-term follow-up (median 36 months, interquartile range 15–80 months) the mean number of antihypertensive agents remained stable at 1.9 ± 1.5 , whereas blood pressure control had improved (mean SBP 129.9 ± 14.9 mm Hg) although this was not statistically significant ($P = .662$). From preoperative to long-term follow-up, the mean reduction in antihypertensive agents was 1.8 ± 1.4 , and mean reduction in SBP was 23.2 ± 23.7 mm Hg.

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