Published in final edited form as:

J Surg Res. 2012 October ; 177(2): 241–247. doi:10.1016/j.jss.2012.07.059.

Persistent hypertension after adrenalectomy for an aldosterone-producing adenoma: weight as a critical prognostic factor for aldosterone's lasting effect on the cardiac and vascular systems

Yvette Carter, M.D., Madhuchhanda Roy, M.D., PhD, Rebecca S. Sippel, M.D., and Herbert Chen, M.D.

Section of Endocrine Surgery, Department of Surgery, University of Wisconsin, Madison, WI

Abstract

Background—Primary aldosteronism caused by an aldosterone producing adrenal tumor/aldosteronoma (APA), is a potentially curable form of hypertension, via unilateral adrenalectomy. Resolution of hypertension (HTN) is not as prevalent after tumor resection, as are the normalization of aldosterone secretion, hypokalemia, and other metabolic abnormalities. Here, we review the immediate and long term medical outcomes of laparoscopic adrenalectomy in patients with an APA, and attempt to identify any distinctive gender differences in the management of resistant hypertension.

Materials and Methods—We performed a retrospective review of the prospective Adrenal database at the University of Wisconsin between January 2001 and October 2010. Of the 165 adrenalectomies performed, thirty-two were for the resection of an aldosteronoma (APA). Patients were grouped according to their post-operative hypertension status. Those patients with normal blood pressure (<120/80 mmHg) and on no anti-hypertensive medication (CURE) were compared to those who continued to require medication for blood pressure control (HTN). We evaluated gender, age, body mass index (BMI), tumor size, duration of time with high blood pressure, and the differences in systolic and diastolic blood pressure following adrenalectomy. Statistical analysis was performed utilizing student's *t* test. Statistical significance was defined as a *p* value < 0.05.

Results—We identified 32 patients with an APA based on biochemical and radiographic studies, two patients were excluded, due to missing data. There were 19 males (63%) and 11 (37%) females, with a mean age was 48.3 ± 2.1 years, and mean tumor size was 24 ± 3 mm. Post-operatively, patients required significantly fewer anti-hypertensive medications (1.5 ± 0.2 vs. 3.3 ± 0.3 , $p < 0.001$). Nine patients (31%) had complete resolution of their hypertension, requiring no post-operative anti-hypertensive medication. The only significant difference between the genders, was a lower BMI in women (27.6 ± 1.7 versus 33.4 ± 2.1 kg/m², $p = 0.04$). 90% of the cohort had at least a 20 mmHg decline in their systolic blood pressure post-operatively, placing them in the pre-hypertensive or normal blood pressure categories. 66% of the CURE patients required at least six months for resolution of their hypertension. All twenty patients who presented with hypokalemia, had immediate resolution post-operatively, and did not require continuance of the pre-operative spironolactone or potassium supplementation.

Conclusions—Laparoscopic adrenalectomy for aldosterone producing adenoma results in the normalization of, or more readily manageable blood pressure in 90% of patients, within six

months. Metabolic disturbances are immediately corrected with tumor resection. Weight is an important contributing factor in resolving hypertension.

Keywords

Aldosteronoma; persistent hypertension; weight; end organ damage

INTRODUCTION

The clinical picture of hypokalemic, renin-independent primary hyperaldosteronism causing drug-resistant hypertension, was first reported by Jerome Conn in 1955 [1]. Traditionally noted to be rare, an APA/aldosteronoma accounts for about 60% of primary hyperaldosteronism [2]. It is the most common cause of secondary hypertension and is often underreported with an incidence of 2–5% [3–8]. The true incidence and prevalence are difficult to assess, due to the inconsistent inclusion of bilateral adrenal hyperplasia in the diagnosis, as well as the increasing number of hypertensive patients meeting the biochemical criteria for aldosteronism [9]. Accounting for 0.05–2.2% of the hypertensive population, Conn's syndrome is one of the few potentially curable causes of hypertension [4, 10–14]. There is a growing body of evidence supporting the significant contribution that aldosterone makes to both the development and severity of hypertension, as well as its prolonged exposure resulting in end organ damage and failure.

Aldosterone most notably increases sodium absorption in the distal tubules and collecting ducts of the kidneys, resulting in increased intravascular volume and increased blood pressure. Cardiac damage results from greater ventricular septum and left ventricular wall thickness increasing myocardial oxygen demand and consumption. Excess aldosterone production by the tumor increases fibrosis in the vasculature and the intraventricular cardiac septum by increasing collagen production in these areas. Left ventricular hypertrophy, vascular remodeling with intima-media thickening, and cardiac fibrosis, along with renal dysfunction as a result of renal arteriosclerosis, direct damage to nephron geometry, and function, are all potential reasons for persistent hypertension despite APA resection [15–17]. Of concern, is the fact that the effects that aldosterone have on the cardiac, renal and vascular systems, are independent of its effects on increasing blood pressure; hence the long term effect of excess aldosterone exposure on these organs, warrants the prompt and correct evaluation, diagnosis and resection of these tumors.

Focusing on APA, the goal of treatment is normalization of aldosterone levels via surgical resection, or by administering mineralocorticoid receptor antagonists to block the effects of aldosterone [2, 18]. Unilateral laparoscopic adrenalectomy is the gold standard treatment [19–21]. Spironolactone and eplerenone, both mineralocorticoid receptor antagonists, effectively address hypokalemia; however they have drawbacks, including: side effects (painful gynecomastia, decreased libido, menstrual abnormalities, and erectile dysfunction), persistent high blood pressure, and minimal or no effect on other metabolic abnormalities caused by aldosteronism. APA resection completely abolishes aldosterone hypersecretion, can result in a significant decrement in systolic blood pressure (–20 to –40mmHg) and can decrease the number of medications required for blood pressure management [22–25]. Tumor resection results in a clinically relevant improvement in blood pressure control, and attenuated cardiac, cerebrovascular and renal failure morbidities, even in those patients who continue to require anti-hypertensive medication.

The question of what lasting effect hyperaldosteronism has on the heart, brain and kidney, has yet to be completely answered. APA resection results in immediate correction of hypokalemia and other clinical and biochemical signs of adrenal hyperfunction in 98%, but

long term blood pressure normalization is evident in only 20–35% [23, 24, 26–30]. These patients are at a higher risk for myocardial infarction, cerebrovascular accident and renal failure than other hypertensive patients. Studies have focused on the lack of resolution hypertension after tumor resection, and the possible predictors of resolution. Noted predictive factors include: female gender, younger age, requiring less than three anti-hypertensive medications for blood pressure control, having a diagnosis of hypertension for fewer than six years, and adenoma size <20mm [24, 26–28, 28, 31, 32]. In addition, excess aldosterone production puts patients at a higher risk of left ventricular hypertrophy, myocardial infarction, cerebrovascular accidents and renal disease [2].

In this study, we sought to elucidate aldosterone's immediate and long term effects on blood pressure and identify any distinctive gender advantages, in patients who underwent laparoscopic adrenalectomy for an APA.

MATERIALS AND METHODS

Between January 2001 and December 2010, 165 adrenalectomies were performed at a single institution. We retrospectively reviewed the thirty-two patients diagnosed with an APA who underwent unilateral adrenalectomy at our institution. Because of insufficient data, 2 patients were excluded from analysis. The remaining 30 patients were analyzed. A review of the University of Wisconsin Prospective Adrenal Surgery Database was performed. Institutional approval was obtained from the local institutional review board.

This study included patients with the diagnosis of APA, based on biochemical laboratory values, radiographic images, selective venous sampling, and confirmed by final pathology. Patients with other adrenal pathologies were excluded. All patients underwent laparoscopic adrenalectomy. Data were collected on patient demographics, pre-operative evaluation (including biochemical hormonal status and imaging studies), operative narrative, and post-operative course. The criteria used to establish the diagnosis were a history of hypertension with or without hypokalemia, in conjunction with confirmatory laboratory values (increased plasma aldosterone level, suppressed renin activity, and aldosterone: renin ratio). Baseline variables obtained through a review of medical records included: age, body mass index (BMI), tumor size, family history, tobacco and alcohol use, number of blood pressure medications prescribed pre- and postoperatively, duration of hypertension, and family history of hypertension. Laboratory data collected included blood levels of aldosterone, potassium, and plasma renin activity. We assessed the degree of improvement in hypertension and correction of hypokalemia after adrenalectomy.

Specific attention was paid to pre- and post-operative blood pressure measurements, pre-operative comorbidities, tumor size, and anti-hypertensive medications. All operations were performed at a tertiary care hospital by experienced endocrine surgeons. Patient charts were investigated to correctly identify the final pathology, including tumor size, adrenal gland cytology, and the immediate and long-term post-operative outcomes. Patients were grouped according to post-operative hypertension status. Patients who had complete resolution of their hypertension (normal blood pressure per the American Heart Association guidelines and requiring no anti-hypertensive medications) with resection of the adenoma (CURE) were compared to the hypertension (HTN) patients, which consisted of patients who had an attenuated (PRE-HTN) and those with no change in their post-operative anti-hypertensive requirement (PERSISTENT).

The principal outcomes included: correction of hypokalemia, decrease in the number and/or dose of anti-hypertensive medication, at least a 20 mmHg decrement in blood pressure (systolic or diastolic), and normal blood pressure (<120/80 mmHg) without blood pressure

medication. The patients were categorized into two groups: normal blood pressure and no medications (CURE) and patients with persistent hypertension, with a decrease in the number or dose of blood pressure medications or no change (HTN). This group was further classified to note those patients whose blood pressure had a positive response to surgery (PRE-HTN), hence required less medication post-operatively, and those who remained hypertensive (PERSISTENT). Mean follow-up time was 10 ± 1.8 years (median=8 years).

To identify differences between the HTN and CURE groups and genders, univariate analysis with *t*-tests were used. Data are expressed as mean $\pm$ SEM, unless otherwise specified. Statistical calculations were completed using statistical software SPSS version 17 (SPSS, Inc., Chicago, IL) and a *p* value < 0.05 was considered to represent statistical significance for all comparisons.

RESULTS

Of the 165 adrenalectomies performed between January 2001 and December 2010, 32 patients underwent unilateral laparoscopic adrenalectomy for an APA. Of the thirty patients analyzed, eleven (37%) were female, and the mean age was 48 ± 2 years, mean tumor size was 24 ± 3 mm and the majority (67%) presented in the left adrenal gland (table 1). Adrenalectomy resulted in a significant decline in systolic blood pressure (161 ± 5 versus 124 ± 3 mmHg, $p < 0.001$), diastolic blood pressure (100 ± 4 versus 79 ± 2 mmHg, $p < 0.001$) and the number of anti-hypertensive medications (3.4 ± 0.3 versus 1.5 ± 0.2 , $p < 0.001$) required for blood pressure control (figure 1).

Twenty (67%) patients presented with co-existing hypokalemia, and all had immediate correction with the addition of spironolactone to the anti-hypertensive medication regimen. Following surgery hypokalemia was resolved in 100% of patients. No one required spironolactone or potassium supplementation. In addition, with tumor resection, all patients who were prescribed spironolactone pre-operatively had an improvement in the management of their blood pressure. Twenty-seven (90%) patients had a positive blood pressure response to adrenalectomy. Nine (30%) patients had normal post-operative blood pressure and required no medications, while 18 (60%) had a decrement in the dose and/or number of anti-hypertensive medications prescribed. No patient had documented renal insufficiency or failure; however, one patient presented with a remote history of a cerebrovascular accident and two patients had evidence of coronary artery disease (history of myocardial infarction and a positive stress echocardiogram). Adrenalectomy resulted in twenty-six (87%) patients being re-stratified in the pre-hypertensive range, and only 4 (13%) having stage I hypertension.

Comparing the CURE and HTN groups, there was no significant difference in gender, age, or use of tobacco or alcohol (table 3). The CURE group had an even gender distribution; however, the majority of men (74%) had persistent, but improved hypertension. The CURE group had significantly smaller tumors (21 ± 3 versus 24 ± 4 mm, $p < 0.001$), body mass index (BMI) (27.5 ± 1.7 versus 33.4 ± 2.1 kg/m², $p = 0.04$), and were prescribed significantly fewer anti-hypertensive medications for pre-operative blood pressure management (2 ± 0.5 versus 4 ± 0.4 , $p = 0.006$). The HTN group had a significantly longer duration of hypertension (10 years versus 5 years, $p = 0.02$). Blood pressures were similar amongst the CURE and HTN groups. Despite still requiring medication for blood pressure control, the two HTN subgroups demonstrated a significant blood pressure response (pre-HTN- $172 \pm 5/105 \pm 6$ mmHg versus $127 \pm 3/79 \pm 3$ mmHg and PERSISTENT- $146 \pm 7/99 \pm 4$ versus $130 \pm 6/85 \pm 5$ mmHg, $p < 0.001$) to APA resection.

Weight (BMI) was the only clinical parameter distinguishing the genders. There was no difference in age, tumor size, or tobacco and alcohol use (table 2). Women weighed significantly less (BMI of 27.6 ± 1.7 versus 33.4 ± 2.1 , $p=0.04$); however, both genders were, on average, categorized as overweight or obese. Despite pre-operative blood pressures being similar, women were prescribed significantly fewer medications for blood pressure control (2.1 ± 0.3 versus 4.1 ± 0.4 , $p<0.001$) (figure 2). Postoperatively, the diastolic and systolic blood pressures were also similar amongst the genders, despite women requiring fewer medications (figure 3). Men on average, were treated twice as long for hypertension as women (10 versus 5.6 years, $p=0.4$) but this was not significant. Interestingly, there were no significant differences in tumor size, pre-operative or post-post-operative blood pressure or medications, when comparing the different body mass indices in each gender (table 4 and table 5).

DISCUSSION

In our series, hypertension resolved at follow-up (1 day to 9.7 years) in nearly one third of patients who underwent unilateral laparoscopic adrenalectomy for an aldosterone-producing adenoma. Resolution of hypertension was associated with female gender, fewer pre-operatively prescribed anti-hypertensive medications and lower BMI. Our hypertension cure rate (30%) was similar to other studies in which these patients required no blood pressure medication to maintain a blood pressure $120/80$ mmHg [22, 25]. Other studies have noted higher cure rates; however, this was with the utilization of a maximum normal blood pressure of $160/95$ mmHg [19, 33, 34]. Our definition of resolution is in line with current hypertension treatment goals [35].

Despite both genders having an average BMI in the overweight or obese range, women weighed significantly less, were almost in the normal weight category (BMI 25kg/m^2), and 45% of women compared to only 21% of men had complete resolution of their hypertension. In addition females required significantly fewer anti-hypertensive medications pre-operatively, to control their blood pressure. The gender advantage for resolution of hypertension was eliminated in those females who had a BMI in the obese or morbidly obese range. Considering the effect that obesity has on vascular arterial stiffness, vessel sensitivity to pressor substances, and aldosterone secretion, it may be more pertinent than female gender being a prognostic factor for cure of hypertension, as noted by others [28, 35]. Several studies have noted requiring two or fewer blood pressure medications for blood pressure management, as another predictor of hypertension outcome [28, 29]. Our results agree with this, as all of the CURE group were on ≤ 2 medications pre-operatively, compared to only 7% of the HTN group, and suggest that females are more responsive to lower doses of medications, and have more readily controlled blood pressure. In addition, females appear to be more responsive and have more readily controllable blood pressure. The amount of adipose tissue in each patient may play a role, as BMI was a prognostic factor between genders and in the CURE group. Weight is a concern, because of the role adipose tissue plays in aldosterone secretion. Obesity is a known contributing factor to increased aldosterone production, as adipose tissue contains factors that function as secretagogues for the hormone [9]. There is a difference in the activity of the renin-angiotensin system, amongst people of varying weights.

Interestingly, the length of time in which they had been diagnosed with hypertension, was significantly longer in the CURE group, suggesting another etiology for hypertension. The majority of our patients carried a hypertension diagnosis for more than six years. Despite this, 90% of our patients were cured or had improved management of their hypertension with removal of the aldosteronoma. This addresses two issues. First, excess aldosterone makes managing high blood pressure more difficult, and hence, early therapy with a

mineralocorticoid receptor antagonist in APA patients and those with resistant hypertension may prove beneficial for blood pressure control, as well as limit end organ damage, as adrenalectomy has been shown to reverse the myocardial changes inflicted by aldosterone [16]. Secondly, the lack of complete resolution of hypertension suggests another etiology for hypertension. APA with concomitant idiopathic hyperaldosteronism or essential hypertension has been suggested, with the majority of cases being secondary to essential hypertension [36].

The majority (70%) of our patients experienced more manageable blood pressure with the pre-operative administration of the mineralocorticoid receptor antagonist, spironolactone, as well as, after tumor resection. Hypokalemia was resolved, and blood pressure more easily controlled. This may be a result of decreased cardiac, vascular and cerebral mineralocorticoid receptor activation. In addition, despite 66% of patients requiring at least six months for a reduction in the number of anti-hypertensive medications, the majority were able to decrease the dose by one-half, within the immediate (<1 month) period. More than likely, our patients have some component of essential hypertension, secondary to the risks factors present (alcohol and tobacco use and obesity). This suggests that in addition to APA resection, lifestyle interventions, including exercising, maintaining an ideal body weight, smoking cessation and minimal alcohol use, are pertinent to the normalization of blood pressure.

In evaluating tumor characteristics, only a minority of our patients had microadenomas (<7mm), which have been reported to secrete higher amounts of aldosterone [37]. There was no difference in size between genders, even though females on average had tumors <20 mm. The CURE group presented with significantly smaller tumors than the HTN group; however, when further evaluating the HTN group, the improved subgroup had tumors comparable in size to the CURE group. In addition, we examined the histopathology of our patients' adrenal glands and tumors. Only one patient had evidence of zona glomerulosa and zona fasciculata hyperplasia and/or nodules, end organ changes evident of the lasting effects of hyperaldosteronism. Again, this suggests the presence of essential hypertension.

Our study has few limitations. First, it is a retrospective review on a prospective database. Due to the rare incidence of aldosteronomas, a prospective study would be difficult, due to the time factor. The small number of patients is comparable to other studies [16, 37, 38]. Despite the length of our study, it was difficult to obtain long term (>2 years) follow up data on some patients. We also excluded the analysis of biochemical and laboratory data, between the groups. Lastly, the small number of patients does not allow more than two subgroups; therefore, conclusions are limited to cure and persistent hypertension, and gender differences.

CONCLUSION

Laparoscopic adrenalectomy for aldosterone producing adenoma results in the normalization of, or more readily manageable blood pressure in 90% of patients, within six months. Metabolic disturbances are immediately corrected with tumor resection. Weight is an important contributing factor in resolving hypertension.

Acknowledgments

We thank Nicholas Yeutter for his contribution to the data collection and editing of this paper.

Supported by NIH/NCI Supplemental Grant RO1CA12115

References

1. Conn JW. Presidential address. Part II. Primary aldosteronism, a new clinical syndrome, 1955. *J Lab Clin Med.* 1990; 116:253–267. [PubMed: 2203856]
2. Al Fehaily M, Duh Q-Y. Clinical manifestation of aldosteronoma. *Surg Clin N Am.* 2004; 84:887–905. [PubMed: 15145241]
3. Young WF Jr. Primary aldosteronism: A common and curable form of hypertension. *Cardiol Rev.* 1999; 7:207–214. [PubMed: 10423672]
4. Young WF Jr. Primary aldosteronism: update on diagnosis and treatment. *The Endocrinologist.* 1997; 7:213–221.
5. Rossi E, Regolisti G, Negro A, et al. High prevalence of primary aldosteronism using captopril plasma aldosterone to renin ratio as a screening test among Italian hypertensives. *Am J Hypertens.* 2002; 15:896–902. [PubMed: 12372677]
6. Rossi GP, Bernini G, Caliumi C, et al. A prospective study of the prevalence of primary aldosteronism in 1,125 hypertensive patients. *J Am Coll Cardiol.* 2006; 48:2293–3000. [PubMed: 17161262]
7. Foragi R, Preti P, Zoppi A, et al. Prevalence of primary aldosteronism among unselected hypertensive patients: a prospective study based on the use of an aldosterone/renin ratio above 25 as a screening test. *Hypertens Res.* 2007; 30:111–117. [PubMed: 17460380]
8. Douma S, Petidis K, Doumas M, et al. Prevalence of primary hyperaldosteronism in resistant hypertension: a retrospective observational study. *Lancet.* 2008; 371:1921–6. [PubMed: 18539224]
9. Calhoun DA. Aldosteronism and hypertension. *Clin J Am Soc Nephrol.* 2006; 1:1039–1045. [PubMed: 17699324]
10. Streeten DH, Tomycz N, Anderson GH. Reliability of screening methods for the diagnosis of primary aldosteronism. *Am J Med.* 1979; 67:403–413. [PubMed: 474586]
11. Lund JO, Nielsen MD, Giese J. Prevalence of primary aldosteronism. *Acta Med Scand Suppl.* 1981; 646:54–57. [PubMed: 7018185]
12. Gordon RD, Stowasser M, Tunny TJ, et al. High incidence of primary aldosteronism in 199 patients referred with hypertension. *Clin Exp Pharmacol Physiol.* 1994; 21:315–318. [PubMed: 7923898]
13. Loh KC, Koay ES, Khaw MC, et al. Prevalence of primary aldosteronism among Asian hypertensive patients in Singapore. *J Clin Endocrinol Metab.* 2000; 85:2854–2859. [PubMed: 10946893]
14. Lim PO, Rodgers P, Cardale K, et al. Potentially high prevalence of primary aldosteronism in a primary care population. *Lancet.* 1999; 353:40. [PubMed: 10023956]
15. Brilla CG, Pick R, Tan LB, et al. Remodeling of the rat right and left ventricles in experimental hypertension. *Circ Res.* 1990; 67:1355–1364. [PubMed: 1700933]
16. Lin YH, Lee HH, Liu KL, et al. TAIPAI Study Group. Reversal of myocardial fibrosis in patients with unilateral hyperaldosteronism receiving adrenalectomy. *Surgery.* 2011; 150(3):526–533. [PubMed: 21514614]
17. Connell JMC, MacKenzie SM, Freel EM, Fraser R, Davies E. A lifetime of aldosterone excess: long-term consequences of altered regulation of aldosterone production for cardiovascular function. *Endocrine Reviews.* 2008; 29:133–154. [PubMed: 18292466]
18. 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. [PubMed: 15001583]
19. Young WF Jr, Klee GG. Primary Aldosteronism. Diagnostic evaluation. *Endocrinol Metabol Clin North Am.* 1988; 17:367–399.
20. Funder JW, Carey RM, Fardella C, et al. Case detection, diagnosis and treatment of patients with primary aldosteronism: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2008; 93:3266–3281. [PubMed: 18552288]
21. Ballian N, Adler JT, Sippel RS, Chen H. Revisiting adrenal mass size as an indication for adrenalectomy. *J Surg Res.* 2009; 156:16–20. [PubMed: 19592028]

22. Lumachi F, Ermani M, Basso SM, et al. Long-term results of adrenalectomy in patients with aldosterone-producing adenomas: multivariate analysis of factors affecting unresolved hypertension and review of the literature. *Am Surg.* 2005; 71:864–869. [PubMed: 16468537]
23. Pang TC, Bambach C, Monaghan JC, et al. Outcomes of laparoscopic adrenalectomy for hyperaldosteronism. *ANZ J Surg.* 2007; 77:768–773. [PubMed: 17685956]
24. Rossi GP, Bolognesi M, Rizzoni D, et al. Vascular remodeling and duration of hypertension predict outcome of adrenalectomy in primary aldosteronism patients. *Hypertension.* 2008; 51:1366–1371. [PubMed: 18347224]
25. Leteavernier E, Peyrard S, Amar L, et al. Blood pressure outcome of adrenalectomy in patients with primary hyperaldosteronism with or without unilateral adenoma. *J Hypertens.* 2008; 26:1816–1823. [PubMed: 18698217]
26. Blumenfeld JD, Sealey JE, Schluskel Y, et al. Diagnosis and treatment of primary aldosteronism. *Ann Int Med.* 1994; 121:877–885. [PubMed: 7978702]
27. Lo CY, Tam PC, Kung AE, et al. Primary aldosteronism. Results of surgical treatment. *Ann Surg.* 1996; 224:125–130. [PubMed: 8757374]
28. 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. [PubMed: 18376197]
29. Sawka AM, Young WF Jr, Thompson GB, et al. Primary aldosteronism: factors associated with normalization of blood pressure after surgery. *Ann Int Med.* 2001; 135:258–261. [PubMed: 11511140]
30. Fukudome Y, Fujii K, Arima H, et al. Discriminating factors for recurrent hypertension in patients with primary aldosteronism after adrenalectomy. *Hypertens Res.* 2002; 25:11–18. [PubMed: 11924716]
31. Goh BK, Tan YH, Yip SK, et al. Outcome of patients undergoing laparoscopic adrenalectomy for primary hyperaldosteronism. *JSLs.* 2004; 80:320–325. [PubMed: 15554273]
32. Giachetti G, Ronconi V, Rilli S, et al. Small tumor size as favorable prognostic factor after adrenalectomy in Conn's adenoma. *Eur J Endocrinol.* 2009; 160:639–646. [PubMed: 19131503]
33. Celen O, O'Brien MJ, Melby JC, Beazley RM. Factors influencing outcome of surgery for primary aldosteronism. *Arch Surg.* 1996; 131:646–50. [PubMed: 8645073]
34. Obara T, Ito Y, Okamoto T, et al. Risk factors associated with postoperative persistent hypertension in patients with primary aldosteronism. *Surgery.* 1992; 112:987–993. [PubMed: 1455323]
35. National high Blood Pressure Education Program. Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Bethesda, MD: Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute; 2003.
36. Brown CA, Bouldin MJ, Blackston JW, et al. Hyperaldosteronism: the internist's hypertensive disease. *Am J Med Sci.* 2002; 324:227–231. [PubMed: 12385496]
37. Kim RM, Lee J, Soh E-Y. Predictors of resolution of hypertension after adrenalectomy in patients with aldosterone-producing adenoma. *J Korean Med Sci.* 2010; 25:1041–1044. [PubMed: 20592896]
38. Murayama T, Kawabe K, Nijima T. Relationship between postoperative blood pressure change and renal pathophysiology in primary aldosteronism. *Urol Int.* 1984; 39:264–269. [PubMed: 6506359]

Figure 1.
Prescribed anti-hypertensive medications before and after adrenalectomy for an APA

Figure 2.
Gender difference in prescribed anti-hypertensive medications

Figure 3.
Pre- and post-operative blood pressure differences between genders

Figure 4.
Pre- and post-operative blood pressure changes in CURE and HTN (pre-HTN and PERSISTENT) patients

Table 1

Characteristics of patients presenting with an aldosteronoma

GENDER (% female)	19 male; 11 female (37%)
AGE (years)	48 ± 2
BMI (kg/m ²)	31 ± 6
TOBACCO USE	58%
ALCOHOL USE	79%
DURATION OF HYPERTENSION DIAGNOSIS (median, years)	8 (range=1 day to 9.7 years)
Clinical parameters of patients and APA	
TUMOR SIZE (mm)	24 ± 3
TUMOR LOCATION (% left)	20 (67%)
# PRE-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	3.4 ± 0.3
# POST-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	1.5 ± 0.3 *
PRE-OPERATIVE SBP (mmHg)	161 ± 5
POST-OPERATIVE SBP (mmHg)	124 ± 3 *
PRE-OPERATIVE DBP (mmHg)	100 ± 4
POST-OPERATIVE DBP (mmHg)	79 ± 2 *
POTASSIUM (mEq/dl)	3.6 ± 0.2
INCIDENCE OF HYPOKALEMIA	67%

* p<0.001 pre-operative versus post-operative

SBP=systolic blood pressure

DBP=diastolic blood pressure

Table 2

Distinctive APA patient gender differences

	MALE	FEMALE	P value
AGE (years)	51 ± 3	44 ± 3	NS
BMI (kg/m ²)	33.4 ± 2.1	27.6 ± 1.7	0.04
TOBACCO USE	63%	46%	NS
ALCOHOL USE	83%	70%	NS
DURATION OF HYPERTENSION DIAGNOSIS (median, years)	10	5.6	NS
Clinical parameters of patients and APA			
TUMOR SIZE (mm)	26 ± 5	19 ± 2	NS
#PRE-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	4.1 ± 0.4	2.1 ± 0.3 [@]	<0.001
# POST-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	2 ± 0.3 [*]	0.6 ± 0.3 [@]	<0.001
PRE-OPERATIVE SBP (mmHg)	168 ± 5	153 ± 10	NS
POST-OPERATIVE SBP (mmHg)	124 ± 3	124 ± 6 [*]	NS
PRE-OPERATIVE DBP (mmHg)	101 ± 4	99 ± 8	NS
POST-OPERATIVE DBP (mmHg)	79 ± 2 [*]	81 ± 5 [*]	NS

* p<0.001 pre-operative versus post-operative

@ p<0.01 male versus female

Table 3

Distinctive differences between CURE and HTN groups, including pre-hypertension and hypertension subgroups

	CURE	HYPERTENSION		P VALUE
		PRE-HTN	PERSISTENT	
GENDER (% female)	56%	22%	66%	NS
AGE (years)	48± 3	49 ± 3	45 ± 5	NS
BMI (kg/m²)	27.5 ± 1.7	32 ± 2.1	39.9 ± 6.6	0.04
TOBACCO USE (%)	56%	67%	0%	NS
ALCOHOL USE (%)	67%	83%	33%	NS
DURATION OF HYPERTENSION	16	10	6	0.02
DIAGNOSIS (median, years)				
TUMOR SIZE (mm)	21 ± 3	22 ± 4	38 ± 2	<0.001
#PRE-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	2 ± 0.5	4.3 ± 0.4	1.7 ± 0.3	0.006
# POST-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	0	2.2 ± 0.2	1.7 ± 0.3	<0.001
PRE-OPERATIVE SBP (mmHg)	143 ± 14	172 ± 5	146 ± 7	NS
POST-OPERATIVE SBP (mmHg)	114 ± 7	127 ± 3 *	130 ± 6 *	NS
PRE-OPERATIVE DBP (mmHg)	90 ± 8	105 ± 6	99 ± 4	NS
POST-OPERATIVE DBP (mmHg)	77 ± 4	79 ± 3 *	85 ± 5 *	NS

* p<0.001 pre-operative versus post-operative

SBP=systolic blood pressure

DBP=diastolic blood pressure

Table 4

Female hypertension status in relation to BMI

	BMI <25	BMI 30–34.9	BMI > 40
AGE (years)	44 ± 4.5	48.5 ± 6.4	36.5 ± 3.5
TUMOR SIZE (mm)	16 ± 2	20 ± 4	25 ± 0
# PRE-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	2 ± 0.4	2 ± 0.4	2.5 ± 0.5
# POST-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	0.6 ± 0.2	0.3 ± 0.2	1.5 ± 0.5
PRE-OPERATIVE SBP	149 ± 12	148 ± 119	170 ± 30
POST-OPERATIVE SBP	122 ± 11	123 ± 10	129 ± 3
PRE-OPERATIVE DBP	85 ± 6	100 ± 9	126 ± 34
POST-OPERATIVE DBP	76 ± 8	83 ± 5	89 ± 1
# CURE	2/5 (40%)	3/4 (75%)	0/2 (0%)
# PRE-HYPERTENSIVE	3/5 (60%)	0/4 (0%)	1/2 (50%)
# HYPERTENSIVE	0/5 (0%)	1/4 (25%)	1/2 (50%)

SBP=systolic blood pressure

DBP=diastolic blood pressure

Table 5

Male hypertension status in relation to BMI

	BMI <25*	BMI 25–29.9	BMI 30–34.9	BMI 35–39.9	BMI 40
AGE (years)	55 ± 3.1	28 ± 0.7	49 ± 4	59 ± 2	43 ± 10
TUMOR SIZE (mm)	24 ± 4	19 ± 6	23 ± 9	35 ± 2	34 ± 16
# PRE-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	3 ± 1.5	4.6 ± 0.7	4 ± 0.9	5.5 ± 2	3.8 ± 1.2
# POST-OPERATIVE ANTI-HYPERTENSIVE MEDICATIONS	0.7 ± 0.7	2.8 ± 0.2	2.2 ± 0.9	1.5 ± 0.5	2 ± 0.4
PRE-OPERATIVE SBP	140 ± 0	186 ± 7	167 ± 10	160 ± 0	164 ± 7
POST-OPERATIVE SBP	117 ± 2	122 ± 2	122 ± 7	129 ± 1	131 ± 9
PRE-OPERATIVE DBP	90 ± 0	103 ± 3	100 ± 81	80 ± 0	109 ± 11
POST-OPERATIVE DBP	74 ± 3	75 ± 4	81 ± 2	68 ± 0	85 ± 5
# CURE	1/3 (33%)	0/5 (0%)	2/5 (40%)	0/3 (0%)	0/4 (0%)
# PRE-HYPERTENSIVE	1/3 (33%)	5/5 (100%)	3/5 (60%)	3/3 (100%)	3/4 (75%)
# HYPERTENSIVE	0/3 (0%)	0/5 (0%)	0/5 (0%)	0/3 (0)	1/4 (25%)

* One patient in this group was not hypertensive pre-operatively, and was not on any medications prior to surgery

SBP=systolic blood pressure

DBP=diastolic blood pressure