A Retrospective Cohort Study on the Treatment Outcome after Unilateral Adrenalectomy among Patients with Aldosterone-Producing Adenoma at the University of Santo Tomas Hospital

Karren L. Antonio, MD,[1] and Bien J. Matawaran, MD[1]

Abstract

Background: Unilateral adrenalectomy is indicated for patients with unilateral primary aldosteronism resulting in normalization of hypokalemia and resolution of hypertension. This study aims to determine the proportion of patients with cure of hypertension and improvement of hypokalemia after unilateral adrenalectomy among patients with aldosterone-producing adenoma and assess the association of preoperative factors with these outcomes.

Methods: This is a retrospective cohort study among patients with aldosterone-producing adenoma who underwent unilateral adrenalectomy with at least one month follow-up after the operation. Patients were selected from admissions to the University of Santo Tomas Hospital from January 2008 to November 2018. The proportion of patients with cure of hypertension and resolution of hypokalemia were determined. Binary logistic regression was used to determine preoperative factors associated with these outcomes.

Results: Twenty-one patients were included in this study. Cure of hypertension was noted in 47.62% and 42.86% of patients within 24 hours of adrenalectomy and on follow-up, respectively. Improvement of hypokalemia was noted in 61.90% of patients within 24 hours of operation while all patients had improvement of hypokalemia on follow-up. Patients without preoperative hypokalemia were more likely to have cure of hypertension within 24 hours of adrenalectomy (OR=0.0250, *p=0.005*) and on follow-up (OR=0.0571, *p=0.010*).

Conclusion: Unilateral adrenalectomy results in improvement of hypertension and hypokalemia in the majority of patients with aldosterone-producing adenoma. Shorter duration of hypertension and absence of preoperative hypokalemia were significantly associated with cure of hypertension after unilateral adrenalectomy.

Keywords: Hyperaldosteronism, Aldosterone-producing adenoma, Adrenalectomy

Introduction

Secondary hypertension brought about by primary aldosteronism is characterized by an excessive autonomous aldosterone production but is a potentially curable form of hypertension. Excess levels of aldosterone enhance sodium reabsorption and potassium excretion causing hypertension and hypokalemia. In previous studies, primary aldosteronism accounted for < 1% of patients with mild to moderate essential hypertension. However, more recent studies noted that primary aldosteronism is much more common than what was previously thought, accounting for > 5% and possibly > 10% of patients with hypertension.[1,2] In a study conducted in a tertiary hospital in the Philippines, six out of nine patients with aldosterone-producing adenoma underwent unilateral adrenalectomy while in another study only thirteen out of seventeen patients identified to have an aldosterone-producing adenoma underwent unilateral adrenalectomy.[3,4]

[1] Section of Endocrinology, Diabetes and Metabolism, University of Santo Tomas Hospital, Manila, Philippines
Corresponding author: Karren L. Antonio, MD
eMail:- renantonio07@gmail.com

Unilateral hypersecretion of aldosterone secondary to an aldosterone-producing adenoma or a unilateral adrenal hyperplasia is surgically curable and guidelines recommend unilateral adrenalectomy for these patients. Medical treatment such as use of a mineralocorticoid receptor antagonist is indicated for patients with unilateral primary aldosteronism who refuse or cannot undergo surgery. If left untreated, persistent elevated levels of aldosterone cause cardiovascular and renal changes which increase the patient's risk for complications.[2]

After adrenalectomy, biochemical cure characterized by normalization of hypokalemia and aldosterone levels is present in almost all patients. Blood pressure is expected to normalize or show maximum improvement one to six months after unilateral adrenalectomy but can continue to decrease until one year postoperatively in some patients. However, resolution of hypertension is not documented in all patients after unilateral adrenalectomy. Multiple risk factors have been suggested to predict persistent hypertension after unilateral adrenalectomy such as age, gender, body mass index, duration of hypertension, family history of hypertension and preoperative number of antihypertensive agents.[5]

There are a number of studies which showed that adrenalectomy among patients with aldosterone-producing adenoma resulted in cure of hypertension or improvement with the use of fewer number of anti-hypertension medications. The proportion of patients with cure of hypertension ranged from 42% to 63% while patients with improvement of hypertension ranged from 50% to 95% in various studies. Preoperative factors noted to be associated with cure of hypertension were also different among the studies. Female sex, BMI ≤ 25 kg/m^2, duration of hypertension ≤ 6 years and use of antihypertensive medications ≤ 2 were parameters associated with cure after unilateral adrenalectomy. Other factors such as preoperative and postoperative blood pressure as well as the number of antihypertensive medications were not able to predict postoperative cure. Persistent hypertension despite successful adrenalectomy with documented biochemical cure can be secondary to persistent cardiovascular and renal changes which occurred during initial delay in the diagnosis and treatment of unilateral primary aldosteronism. In addition, development of essential hypertension or another disorder associated with hypertension such as chronic kidney disease may account for the persistent elevations in blood pressure after adrenalectomy. On the other hand, 98-100% of patients with aldosterone-producing adenoma who underwent unilateral adrenalectomy had normalization of hypokalemia after the operation. Postoperative levels of potassium were not influenced by any of the predictors investigated.[6-12]

Zarnegar et al. developed an Aldosteronoma Resolution Score which is a prediction model used to identify patients with aldosterone-producing adenoma who are more likely to have resolution of hypertension after unilateral adrenalectomy using data readily available on initial presentation. The predictors were: use of ≤ 2 antihypertensive medications, BMI ≤ 25 kg/m^2, duration of hypertension of ≤ 6 years and female sex. Their analysis showed that a higher Aldosteronoma Score is associated with an increased likelihood of resolution of hypertension after unilateral adrenalectomy. There are studies which used this prediction model in different populations and they found that an Aldosteronoma Resolution Score of 3 to 5 were associated with resolution of hypertension. However, on further analysis of its individual components, only duration of hypertension of ≤ 6 years, female sex and use of ≤ 2 antihypertensive medications were found to be independent predictors of resolution of hypertension among patients with aldosterone-producing adenoma after unilateral adrenalectomy.[12-14]

There is limited local data on the proportion of patients with primary hyperaldosteronism who underwent unilateral adrenalectomy who have persistent hypertension and postoperative hypokalemia. This may be important because other studies report that there are various somatic mutations causing aldosterone-producing adenoma and the prevalence of each mutation varies depending on ethnicity. Studies also showed that some somatic mutations may be associated with severity of disease as well as postoperative cure of hypertension.[15]

This study therefore aims to determine the proportion of patients with cure of hypertension and improvement of hypokalemia after unilateral adrenalectomy among Filipino patients with aldosterone-producing adenoma and assess association of preoperative factors with these outcomes.

Methodology

This study was carried out in accordance with the applicable International Conference on Harmonization Guidelines on Good Clinical Practice Guidelines (ICH-GCP) and was conducted once approved by the UST Hospital Institutional Review Board. All patient information and records included in the study were held in strict confidence.

Research Design and Study Population. This is a retrospective cohort study of patients with aldosterone-producing adenoma who underwent unilateral adrenalectomy. Patients were selected from admissions to the University of Santo Tomas Hospital from January 2008 to November 2018 using purposive sampling technique. This study included patients, aged 18 years and above, with aldosterone-producing adenoma documented by an aldosterone to renin ratio of ≥ 20 ng/dL and an adrenal CT scan identifying a unilateral tumor, who had undergone unilateral adrenalectomy. The duration of follow-up was determined from the date unilateral adrenalectomy was performed to the last date of follow-up in the clinic. Patients were included if at least one month had elapsed since the time of initial treatment to ensure a minimum of one month of follow-up. Patients who underwent partial adrenalectomy or debulking were

Table I. Demographic, Clinical and Biochemical Features of Patients with Aldosterone-Producing Adenoma Pre- and Post-Unilateral Adrenalectomy

Parameter	Mean ± SD	
	Preoperative	≥1 month after Adrenalectomy
Age	37.5 ± 8.4	38.2 ± 8.5
Duration of Hypertension (months)	62.3 ± 42.9	*
Duration of follow-up (months)	10.8 ± 17.8	*
Highest Systolic Blood Pressure (mmHg)	182.4 ± 26.8	*
Highest Diastolic Blood Pressure (mmHg)	108.1 ± 18.9	*
Nadir Potassium (mmol/L)	2.6 ± 0.6	*
Size of Adenoma (cm)	2 ± 0.9	*
Body mass index (kg/m^2)	24.0 ± 4.0	24.1 ± 4.1
Systolic Blood Pressure (mmHg)	129 ± 7.7	126 ± 11.5
Diastolic Blood Pressure (mmHg)	80 ± 7.7	78 ± 7.3
Number of Antihypertensive Medications	2.4 ± 0.9	0.8 ± 0.8
Serum Potassium (mmol/L)	3.9 ± 0.4	4 ± 0.3
Serum Creatinine (mg/dL)	0.9 ± 0.3	*
Glomerular Filtration Rate (mL/min/1.73m^2)	94 ± 26	*
Plasma Renin Activity (ng/mL/hr)	0.2 ± 0.2	*
Plasma Aldosterone Concentration (ng/dL)	48.9 ± 50	*
Aldosterone to Renin Ratio	474.4 ± 825.5	*

excluded from this study. Patients who did not return for follow-up at least one month after unilateral adrenalectomy and patients without postoperative serum potassium level were also withdrawn from this study. Patients with missing data were also excluded from the study.

Charts and medical records of patients who fulfilled the inclusion criteria were retrieved and reviewed. The following baseline parameters before unilateral adrenalectomy were recorded: age, sex, duration of hypertension, number of antihypertensive medications, BMI, blood pressure, size of adenoma, preoperative serum potassium, nadir serum potassium level, serum creatinine, glomerular filtration rate, plasma aldosterone concentration, plasma renin and aldosterone to renin ratio. The following parameters 24 hours after operation and at least one month after unilateral adrenalectomy were also recorded: number of antihypertensive medications, blood pressure and serum potassium.

In this study, cure of hypertension was defined as a blood pressure < 140/90 mmHg without antihypertensive medications. Improvement of hypertension was defined as a reduction in the number of antihypertensive medications needed to maintain a blood pressure level < 140/90 mmHg. Patients who did not satisfy any of the above definitions were considered to have no improvement in hypertension.

The number of antihypertensive medications before and after unilateral adrenalectomy were noted to determine if there was a reduction in the number of antihypertensive medications needed to maintain a blood pressure < 140/90 mmHg.

Patients taking potassium supplements prior to unilateral adrenalectomy were defined to have preoperative hypokalemia. Patients on mineralocorticoid antagonist with preoperative potassium level of 3.6 mmol/L before initiating the said medication were also defined to have preoperative hypokalemia. Nadir potassium was defined as the lowest serum potassium level documented during the patient's preoperative work-up. Postoperative hypokalemia was defined as a serum potassium level < 3.5 mmol/L any time after unilateral adrenalectomy. Improvement of hypokalemia was defined as a potassium level ≥ 3.5 mmol/L without potassium supplements.

Data Analysis. Data were reported as mean ± SD or median with range for continuous data. Categorical data were reported as percentages. The proportion of patients with cure of hypertension and postoperative hypokalemia after unilateral adrenalectomy were determined. Paired *t-test* was used to compare parameters before and after adrenalectomy. To determine biochemical risk factors associated with cure of hypertension or resolution of hypokalemia after unilateral adrenalectomy, binary univariate logistic regression was applied. *Student's t-test* was used in the univariate analysis. Univariate logistic regression was used to determine association of preoperative hypokalemia and cure of hypertension. Given the small sample size, reported odds ratio (OR) are only crude values. Statistically significant difference was decided based on $p < 0.05$. *Medcalc® Statistical Software version 19.2.6* (MedCalc Software Ltd, Ostend, Belgium) was used to carry-out statistical analysis.

Results

For the years 2008-2018, a total of 37 patients were identified to have primary hyperaldosteronism secondary to aldosterone-producing adenoma and 23 (62.16%) of these patients underwent unilateral adrenalectomy. Two patients were excluded from this study because of incomplete data. A total of 21 patients were included and majority of the patients included are female (81%). The presence of hypertension with hypokalemia (71.34%) was the most common indication for screening of primary aldosteronism. Other indications included hypertension at a young age (14.29%), poorly controlled hypertension (9.52%) and work-up for adrenal incidentaloma (4.76%). Majority of patients were on two antihypertensive medications (57.14%) while 33.33% of patients were on three or more antihypertensive medications. The most commonly used antihypertensive agent is spironolactone (80.95%). Preoperative hypokalemia was noted in 57.14% of patients. Laparoscopic adrenalectomy was done in 17 out of 21 patients (80.95%) while the remaining four patients underwent open adrenalectomy. Aldosterone-

Table II. Association of Preoperative Hypokalemia and Hypertension among Patients with Aldosterone-Producing Adenoma who underwent Unilateral Adrenalectomy

Parameter	Without Cure of Hypertension	With Cure of Hypertension	Odds Ratio	p value
Within 24 Hours of Unilateral Adrenalectomy				
Without Preoperative Hypokalemia	1	8	0.0250	0.005*
With Preoperative Hypokalemia	10	2		
≥1 Month After Unilateral Adrenalectomy				
Without Preoperative Hypokalemia	2	7	0.0571	0.010*
With Preoperative Hypokalemia	10	2		

**Significant at $p < 0.05$*

Table III. Risk Factors Associated with Cure of Hypertension ≥1 month after Unilateral Adrenalectomy

Parameter	With Cure of Hypertension	Without Cure of Hypertension	t-test p-value	Odds Ratio	
				OR	p value
Age (years), Mean ± SD	33.1 ± 6.4	40.8 ± 8.4	0.0145*	0.87	0.0519
Duration of Hypertension (months)	37.3 ± 18.4	81 ± 46.9	0.0051*	0.97	0.0386*
Number of Antihypertensive Medications	2.1 ± 0.6	2.6 ± 1.1	0.1100	0.50	0.2583
Body mass index (kg/m^2), Mean ± SD	23.2 ± 3.9	24.5 ± 4.1	0.2416	0.92	0.4658
Preoperative Systolic Blood Pressure (mmHg)	127.8 ± 6.7	130 ± 8.5	0.2555	0.96	0.5045
Preoperative Diastolic Blood Pressure (mmHg)	80 ± 8.7	80 ± 7.4	0.0031*	1.00	1.0000
Size of Adenoma (cm)	2 ± 0.7	1.9 ± 1.1	0.4556	1.06	0.9101
Serum Potassium (mmol/L)	4 ± 0.4	3.8 ± 0.3	0.2329	2.68	0.4289
Nadir Potassium (mmol/L)	2.8 ± 0.7	2.5 ± 0.6	0.1560	2.24	0.2903
Serum Creatinine (mg/dL)	0.8 ± 0.2	1 ± 0.4	0.0644	0.07	0.1923
Glomerular Filtration Rate (mL/min/1.73m^2)	103.7 ± 16.4	86.7 ± 29.9	0.0571	1.03	0.1515
Plasma Renin Activity (ng/mL/hr)	0.3 ± 0.2	0.2 ± 0.2	0.1557	23.39	0.2861
Plasma Aldosterone Concentration (ng/dL)	44.8 ± 36.4	52 ± 59.6	0.3693	1.00	0.7417
Aldosterone to Renin Ratio	224.8 ± 172.3	661.6 ± 1062.1	0.0936	1.00	0.3168

** Significant at $p < 0.05$*

producing adenoma was more commonly located on the left adrenal gland (61.9%). Histopathology results for all patients revealed adrenocortical adenoma. Mean follow-up time was 10.8 months with a range of 1 to 73 months. Other baseline characteristics of patients are summarized in *Table I*.

Although we were unable to document a significant reduction in the systolic (*p=0.1349*) and diastolic (*p=0.2393*) blood pressure at least one month after unilateral adrenalectomy, there was a significant reduction in the number of antihypertensive medications used preoperatively when compared to the number being used at least one month after the operation with a mean of 2.2 ± 0.6 and 0.8 ± 0.8, respectively (*p<0.001*). Within 24 hours of unilateral adrenalectomy, cure of hypertension was seen in 47.62% of patients while improvement of hypertension was seen in 33.33% of patients. No improvement in hypertension was noted in 19.05% of patients. On follow-up, at least one month after unilateral adrenalectomy, 42.86% of patients were noted to have been cured of hypertension while improvement of hypertension was seen in 42.86% of patients. No improvement in hypertension was noted in 14.29% of patients. The percentage of patients requiring three or more antihypertensive medications on follow-up was reduced from 33.33% to none. Improvement of hypokalemia was noted in 61.90% of patients within 24 hours of unilateral adrenalectomy while 100% of patients had improvement of hypokalemia on follow-up at least one month after unilateral adrenalectomy.

The presence of preoperative hypokalemia was significantly associated with cure of hypertension after unilateral adrenalectomy (*Table II*). A lower proportion of patients with cure of hypertension had preoperative hypokalemia within 24 hours of unilateral adrenalectomy (20.0% vs. 90.0%, *p<0.002*) and on follow-up at least one month after unilateral adrenalectomy (22.2% vs. 83.3%, *p=0.009*). Patients with preoperative hypokalemia would have a 97.5% decrease in odds of cure of hypertension than those without preoperative hypokalemia within 24 hours of unilateral adrenalectomy (crude OR=0.0250, *p=0.005*) and 94.3% reduction in odds of cure of hypertension on follow-up at least one month after unilateral adrenalectomy (crude OR=0.0571, *p=0.010*). Of the nine patients without preoperative hypokalemia, only one was without cure of hypertension within 24 hours of unilateral adrenalectomy but on follow-up at least one month after unilateral adrenalectomy, one other patient who was previously identified with cure of hypertension within 24 hours of operation changed status to without cure of hypertension. This may be caused by the development of essential hypertension or other diseases associated with hypertension such as chronic kidney disease in the years following unilateral adrenalectomy.

Table IV. Risk Factors Associated with Cure of Hypertension within 24 hours of Unilateral Adrenalectomy

Parameter	With Cure of Hypertension	Without Cure of Hypertension	t-test p-Value	Odds Ratio	
				OR	p value
Age (years) , mean±SD	35.1 ± 7.8	39.6 ± 8.7	0.1109	0.93	0.2196
Duration of Hypertension (months),mean±SD	48 ± 29.4	75.3 ± 50.1	0.0716	0.98	0.1525
Number of Antihypertensive Medications (preoperative)	2.2 ± 0.6	2.5 ± 1.1	0.1971	0.63	0.3925
Body mass index (kg/m^2)	23.7 ± 3.9	24.2 ± 4.2	0.3903	0.97	0.7700
Preoperative Systolic Blood Pressure (mmHg)	127 ± 6.7	130.9 ± 8.3	0.1249	0.93	0.2431
Preoperative Diastolic Blood Pressure (mmHg)	79 ± 8.8	80.9 ± 7	0.2953	0.97	0.5669
Size of Adenoma (cm)	1.8 ± 0.6	2.1 ± 1.1	0.2209	0.66	0.4393
Preoperative Serum Potassium (mmol/L)	4.1 ± 0.4	3.7 ± 0.3	0.0147*	31.25	0.0576
Nadir Potassium (mmol/L)	2.9 ± 0.7	2.4 ± 0.6	0.0524	3.75	0.1091
Serum Creatinine (mg/dL)	0.8 ± 0.2	1 ± 0.4	0.0422*	0.03	0.1257
Glomerular Filtration Rate (mL/min/1.73m^2)	105.1 ± 15.6	83.9 ± 29.9	0.0288*	1.04	0.0816
Plasma Renin Activity (ng/mL/hr)	0.3 ± 0.2	0.2 ± 0.2	0.0959	56.2	0.1855
Plasma Aldosterone Concentration (ng/dL)	41.2 ± 36.4	56 ± 60.7	0.2519	0.99	0.5007
Aldosterone to Renin Ratio	177.1 ± 148.8	744.7 ± 1083.6	0.0575	0.997	0.2457

**Significant at p < 0.05*

Table V. Risk Factors Associated with Postoperative Hypokalemia within 24 hours of Unilateral Adrenalectomy

Parameter	With Postoperative Hypokalemia	Without Postoperative Hypokalemia	t-test p value	Odds Ratio	
				OR	p value
Age (years), Mean ± SD	40.9 ± 4.2	35.4 ± 9.7	0.0456	1.09	0.1581
Duration of Hypertension (months), Mean ± SD	84 ± 47.6	48.9 ± 35.1	0.0484	1.02	0.0807
Number of Antihypertensive Medications	2.3 ± 0.5	2.5 ± 1.1	0.2782	0.76	0.6040
Body mass index (kg/m^2), Mean ± SD	23.7 ± 3.1	24.2 ± 4.5	0.3843	0.97	0.7743
Preoperative Systolic Blood Pressure (mmHg)	130 ± 7.6	128.5 ± 8	0.3320	1.03	0.6491
Preoperative Diastolic Blood Pressure (mmHg)	80 ± 7.6	80 ± 8.2	0.5000	1.00	1.0000
Size of Adenoma (cm)	2 ± 0.7	1.9 ± 1.1	0.4005	1.13	0.8091
Serum Potassium (mmol/L)	3.7 ± 0.4	4 ± 0.4	0.1007	0.15	0.1930
Nadir Potassium (mmol/L)	2.4 ± 0.4	2.8 ± 0.7	0.1068	0.43	0.2660
Serum Creatinine (mg/dL)	1 ± 0.4	0.8 ± 0.3	0.1968	4.05	0.3369
Glomerular Filtration Rate (mL/min/1.73m^2)	83.7 ± 28.2	100.3 ± 23.4	0.0925	0.97	0.1628
Plasma Renin Activity (ng/mL/hr)	0.2 ± 0.1	0.2 ± 0.2	0.4041	0.48	0.8038
Plasma Aldosterone Concentration (ng/dL)	49.6 ± 30	48.5 ± 60.3	0.4767	1.00	0.9574
Aldosterone to Renin Ratio	421 ± 447.7	507.3 ± 1007.8	0.3956	1.00	0.8125

**Significant at p < 0.05*

Univariate analysis showed that duration of hypertension was statistically significant in predicting cure of hypertension at least one month after unilateral adrenalectomy (crude OR=0.66, *p=0.0386*). A trend suggesting that a younger age was associated with cure of hypertension at least one month after unilateral adrenalectomy was noted but this did not reach statistical significance (t*(df)* = -2.36 (19), *p=0.0145*, crude OR=0.87, *p=0.0519*). No other variables were noted to significantly affect cure or improvement of hypertension within 24 hours or at least one month after unilateral adrenalectomy (*Table III and IV*).

A trend suggesting an association between duration of hypertension and hypokalemia within 24 hours of unilateral adrenalectomy was noted but did not reach statistical significance (t*(df)*= 1.80 (12), *p=0.0484*, crude OR=1.30, 95%CI=0.97-173, p=0.0807). No other variables were noted to significantly affect resolution of hypokalemia within 24 hours of unilateral adrenalectomy (*Table V*).

Discussion

Normalization of blood pressure and resolution of hypokalemia are the major parameters assessed among patients with aldosterone-producing adenoma who underwent unilateral adrenalectomy. Similar to the study by Ebison et. al., we were unable to document a significant reduction in systolic and diastolic blood pressure.[7] Patients were already on antihypertensive medications when systolic and diastolic blood pressures were measured preoperatively which may be the reason we were unable to appreciate a significant reduction in systolic and diastolic blood pressure. A significant reduction in the number of antihypertensive medications needed to control blood pressure was noted suggesting a better control of blood pressure after unilateral adrenalectomy. In our study, normalization of blood pressure without the aid of any antihypertensive medication on follow-up was achieved in 42.86% of patients which was comparable to other studies wherein cure was documented in 42% to 63% of patients.[6-12] We also documented an improvement of hypertension in

42.86% on follow-up of patients which is lower compared to other studies conducted which documented an improvement of hypertension on 50% to 95% of patients.[6-12] Multiple factors such as age, female gender, body mass index, duration of hypertension, family history of hypertension and number of medications were suggested to predict the risk of persistent hypertension in previous studies. Similar to other studies, we identified a shorter duration of hypertension as a predictor of cure of hypertension after unilateral adrenalectomy (crude OR=0.66, 95%CI=0.45-0.98, *p=0.0386*). However, we failed to identify other risk factors which could significantly predict cure of hypertension at least one month after unilateral adrenalectomy.

In contrast to other studies, we documented a cure of hypertension and improvement of hypertension in 47.62% and 33.33% of patients, respectively within 24 hours of unilateral adrenalectomy. This indicates that in some patients, antihypertensive medication is no longer required immediately after the operation. Given that not all the patients demonstrated normalization of blood pressure immediately after unilateral adrenalectomy, preoperative factors which could significantly predict normalization of blood pressure within 24 hours of unilateral adrenalectomy would be highly useful. Unfortunately, we were unable to identify other preoperative factors which could aid us in identifying patients likely to have normalization of blood pressure within 24 hours of unilateral adrenalectomy.

In our study, 38.1% of patients were sent home with potassium supplements after unilateral adrenalectomy. This was comparable to another study wherein 35.29% of patients were sent home with potassium supplements after the operation.[3] Although aldosterone hypersecretion typically resolves after adrenalectomy, non-resolution of hypokalemia immediately after adrenalectomy may be due to the time needed to normalize the endocrine environment. In a study done by Takamatsu et al. only 79% was found to have complete biochemical success, defined as normalization of serum potassium and aldosterone to renin ratio, a month after adrenalectomy.[16] They noted that despite the significant decrease in plasma aldosterone a month after operation, plasma renin may remain low resulting in a persistently elevated aldosterone to renin ratio. We were unable to measure plasma aldosterone and renin postoperatively which may have permitted the identification of possible factors influencing non-resolution of hypokalemia within 24 hours of adrenalectomy, thus limiting our study.

Patients who were sent home with potassium supplements were noted to have normal potassium levels without potassium supplementation on postoperative follow-up accounting for the documented 100% resolution of hypokalemia at least one month after unilateral adrenalectomy. This was similar to other studies which documented resolution of hypokalemia on postoperative follow-up in 98% to 100% of patients.[6-12]

In our study hypertension with hypokalemia was the most common indication for screening for primary hyperaldosteronism despite the fact that more recent studies show that only 9-34% of patients with primary hyperaldosteronism present with hypokalemia. Our study noted a significant association between the absence of preoperative hypokalemia and cure of hypertension after unilateral adrenalectomy. This highlights the importance of identifying patients with primary hyperaldosteronism without hypokalemia because they were identified to have a higher probability of cure of hypertension after unilateral adrenalectomy for aldosterone-producing adenoma. According to Funder et al., apart from hypertension associated with hypokalemia, aldosterone-producing adenoma should be suspected among patients presenting with sustained blood pressure ≥150/100 mmHg, hypertension despite three antihypertensive medications including a diuretic, blood pressure controlled on four or more antihypertensive medications, hypertension in the presence of an adrenal incidentaloma, hypertension with sleep apnea, elevated blood pressure with a family history of onset of hypertension and cerebrovascular accident at less than 40 years of age and all first-degree relatives of patients with hyperaldosteronism.[2] Given that patients without preoperative hypokalemia were found to have a higher probability of normalization of blood pressure, this also suggests that severity of hyperaldosteronism can influence the resolution of hypertension after unilateral adrenalectomy. However, we were unable to document a significant association between adenoma size, plasma aldosterone level or aldosterone to renin ratio and cure of hypertension after unilateral adrenalectomy.

Despite the documented cure of hypertension and resolution of hypokalemia after unilateral adrenalectomy in our study, we were still unable to identify preoperative factors which could sufficiently predict these outcomes. In addition, our small sample size only enables us to make crude associations on the preoperative factors affecting cure of hypertension and improvement of hypokalemia, therefore limiting our study. Further studies with a larger sample size are warranted to allow multivariate analysis. We also recommend measurement of plasma aldosterone and renin to document biochemical cure and to aid in identifying more factors influencing the cure of hypertension and postoperative hypokalemia within 24 hours and on follow-up at least one month after unilateral adrenalectomy.

A study which was conducted in Korea revealed that a specific mutation was associated with cure of hypertension after unilateral adrenalectomy among patients with aldosterone-producing adenoma.[15] We were unable to perform an analysis for mutations which could predict or be associated with certain outcomes after adrenalectomy, thus limiting our study. Identification of the specific genetic mutation present among Filipino patients with aldosterone-producing adenoma may be done to identify patients with a higher probability of cure of hypertension after unilateral adrenalectomy. Identification of the specific mutation may further aid us in properly identifying patients who

will need further medications after unilateral adrenalectomy

Conclusion

Unilateral adrenalectomy results in improvement of hypertension and improvement of hypokalemia in majority of patients with aldosterone-producing adenoma. Shorter duration of hypertension and absence of preoperative hypokalemia were significantly associated with cure of hypertension after unilateral adrenalectomy.

Conflict of Interest. No potential conflict of interest relevant to this article was reported. This research received no specific grant from any funding agency.

References

1. Shariq OA, Bancos I, Cronin PA, Farley DR, Richards ML, Thompson GB, et al. Contralateral suppression of aldosterone at adrenal venous sampling predicts hyperkalemia following adrenalectomy for primary aldosteronism. Surgery 2018;163:183-190.
2. Funder JW, Carey RM, Mantero F, Murad MH, Reincke M, Shibata H, et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology and Metabolism 2016; 101:1-30.
3. Doroin YS, Gomez HS, Mercado-Asis L. Clinical Profile of Patients with Primary Hyperaldosteronism Secondary to Adrenal Adenoma. Philippine Journal of Internal Medicine 2003; 41:18-22.
4. Gimeno CA, Acampado LT. Clinical Profile of Patients with Primary Hyperaldosteronism Admitted to the University of the Philippines-Philippine General Hospital (UP-PGH) From 1993 to 2000. Philippine Journal of Internal Medicine 2004; 42:9-15.
5. Zhou Y, Zhang M, Ke S, Liu L. Hypertension Outcomes of Adrenalectomy in patients with primary aldosteronism: a systematic review and meta-analysis. Biomed Central Endocrine Disorders 2017; 17:61.
6. Benham JL, Eldoma M, Khokhar B, Roberts DJ, Rabi DM, Kline GA. Proportion of Patients with Hypertension Resolution Following Adrenalectomy for Primary Aldosteronism: A Systematic Review and Meta-Analysis. The Journal of Clinical Hypertension 2016;18(12):1205-1212.
7. Ebison AV, Isip JQ, De Guzman ML, Aragon JB, Prodigalidad JV. Outcomes Following Laparoscopic Adrenalectomy as Treatment for Patients with Adrenal Nodules. Philippine Journal of Internal Medicine 2016;54(3):1-9.
8. Hu YH, Wu CH, Er LK, Lin CD, Liu YB, Chueh SC, et al. Laparoscopic Single-site Adrenalectomy in Patients with Primary Hyperaldosteronism: a Prospective Study with Long-term Follow-up. Asian Journal of Surgery 2015; xx:1-6.
9. Hannon MJ, Sze WC, Carpenter R, Parvanta L, Matson M, Sahdev A, et al. Clinical Outcomes following Unilateral Adrenalectomy in Patients with Primary Aldosteronism. An International Journal of Medicine 2016;0(0):1-5.
10. Pasquier L, Kirouani M, Fanget F, Nomine C, Caillard C, Arnault V, et. al. Assessment of the Aldosteronoma Resolution Score as a Predictive Resolution Score of Hypertension after Adrenalectomy for Aldosteronoma in French Patients. Langenbecks Archive Surgery 2017.
11. Jonsdottir G, Gudmundsson J, Birgisson G, Sigurjonsdottir HA. Primary Aldosteronism: from Case Detection to Histopathology with up to 6years of Follow-up. Journal of Clinical Hypertension 2017; 19:424-430.
12. Loh WJ, Lim DS, Loh LM, Kek PC. Factors Associated with Resolution of Hypertension after Adrenalectomy in Patients with Primary Aldosteronism. Endocrinology and Metabolism 2018; 33:355-363.
13. Zarnegar R, Young WF, Lee J, Sweet MP, Kebebew E, Farley DR, et. al. The Aldosteronoma Resolution Score: Predicting Complete Resoution of Hypertension After Adrenalectomy for Aldosteronoma. Annals of Surgery 2008;247(3):511-518.
14. Utsumi T, Kawamura K, Imamoto T, Kamiya N, Komiya A, Suzuki S, et. al. High Predictive Accuracy of Aldosteronoma Resolution Score in Japanese Patients with Aldosterone-Producing Adenoma. Surgery 2012; 151:437-443.
15. Hong AR, Kim JH, Song YS, Lee KE, Seo SH, Seong MW, et. Al. Genetics of Aldosterone-Producing Adenoma in Korean Patients. Public Library of Science 2016;11(1):1-9.
16. Takamatsu K, Takeda T, Hattori S, Tanaka N, Morita S, Matsumoto K, et. al. Appropriate Timing for a Biochemical Evaluation After Adrenalectomy for Unilateral Aldosterone-Producing Adenoma. Clinical Endocrinology. 2020; 92(6):503-508.