



## Aldosterone level after saline infusion test could predict clinical outcome in primary aldosteronism after adrenalectomy



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### ARTICLE INFO

#### Article history:

Accepted 1 May 2019

Available online 15 June 2019

### ABSTRACT

**Background:** The saline infusion test is widely used as a confirmatory test for primary aldosteronism, and we hypothesized that post-saline–infusion test aldosterone levels might predict the clinical outcomes in primary aldosteronism patients after adrenalectomy.

**Methods:** An observational cohort study was performed. We included primary aldosteronism patients who had undergone adrenalectomy from the Taiwan Primary Aldosteronism Investigation database between 1995 and 2017. The patients were divided into the following 2 groups: the clinical success group and the resist hypertension group, according to the criteria from the Primary Aldosteronism Surgery Outcome consensus.

**Results:** We enrolled 236 patients with primary aldosteronism (male, 41.1%; mean age, 49.8 years). A total of 79.7% patients achieved clinical success after adrenalectomy after 12-month follow-up. The clinical success group had higher mean blood pressure, higher aldosterone-to-renin ratio, lower potassium, and lower renin levels than that of the resist hypertension group. In multivariate logistic regression analysis, post saline–infusion test aldosterone levels higher than 48 ng/dL (odds ratio, 2.51; 95% confidence interval, 1.04–6.06;  $P = .040$ ), body mass index less than 25 kg/m<sup>2</sup> (odds ratio, 2.22; 95% confidence interval, 1.12–4.40;  $P = .023$ ) and mean blood pressure higher than 115 mmHg (odds ratio, 2.79; 95% confidence interval, 1.37–5.68;  $P = .005$ ) could predict better clinical success rates after adrenalectomy in primary aldosteronism patients.

**Conclusion:** Our study demonstrated that the post-saline–infusion test aldosterone level could not only confirm primary aldosteronism but also forecast clinical outcomes in primary aldosteronism patients after adrenalectomy.

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### Introduction

Primary aldosteronism (PA), characterized by an inappropriate production of aldosterone, is the most common form of secondary hypertension (HTN).<sup>1,2</sup> The prevalence of PA is reported to be 5% in the general HTN population<sup>3</sup> and is increasing to 15%–20% in refractory hypertension patients.<sup>2</sup> Several studies have demonstrated that higher cardiovascular and cerebrovascular morbidity and mortality rates were observed in PA patients compared with essential HTN patients after matching age, sex, and blood

Supported by Taiwan National Science Council (101-2314-B-002-085-MY3, 102-2314-B-002-140-MY2, 104-2314-B-002-125-MY3, 106-2314-B-002-166-MY3, 107-2314-B-002-026-MY3), National Health Research Institutes (PH-102-SP-09), National Taiwan University Hospital (106-FTN20, 106-P02, UN106-014, 106-S3582, 105-P05, VN105-04, 105-S3061, 107-S3809, 107-T02), and Ministry of Science and Technology (MOST) of the Republic of China ([Taiwan] MOST 106-2321-B-182-002).

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<https://doi.org/10.1016/j.surg.2019.05.001>

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pressure.<sup>4–7</sup> In addition, PA patients are found to be associated with adverse metabolic risks, including insulin resistance, type 2 diabetes mellitus, and osteoporosis.<sup>8–10</sup> Targeted treatment with adrenalectomy or mineralocorticoid receptor antagonist can improve the outcome of PA patients.<sup>11,12</sup> Although adrenalectomy is currently the standard treatment in aldosterone-producing adenoma (APA) patients,<sup>13,14</sup> some patients still have high blood pressure (BP) or need anti-HTN medications after adrenalectomy.

Recommendations for treatment of PA are hampered by the lack of randomized trials, and therefore it is an important and difficult issue to determine the patients who might have better clinical outcomes and the patients who might gain more benefit from adrenalectomy. To evaluate the outcome after adrenalectomy treatments, the Primary Aldosteronism Surgical Outcome (PASO) study<sup>15</sup> reached consensus by experts worldwide regarding clinical and biochemical outcome. Clinical success was based on BP and use of antihypertensive drugs, while biochemical success was based on plasma potassium, aldosterone and renin level.

Saline-infusion test (SIT) is one of the most widely used confirmatory tests for PA because of its practicability, costs, and compliance. The post-SIT aldosterone level is not only a physiologic response to the diagnosis of PA but also an indication of disease severity.<sup>16</sup> Patients with higher post-SIT aldosterone levels had higher systolic BP, lower serum potassium (K), and higher 24-h urine albumin excretion at diagnosis. In addition, patients with higher post-SIT aldosterone may also have a significantly better outcome after adrenalectomy treatment.<sup>16</sup>

To find PA patients who would derive the most benefit from an adrenalectomy, we examined the potential predictors forecasting clinical outcome. We hypothesized that post-SIT aldosterone levels could be a predictor of clinical outcome in PA patients after adrenalectomy.

## Methods

### Patients

This is an observational cohort study, and we enrolled 236 patients diagnosed with PA from 1995 to 2017, all of whom had undergone treatment with adrenalectomy and were registered in the Taiwan Primary Aldosteronism Investigation (TAIPAI) database.<sup>14,17–24</sup> Consent had been obtained from each patient or subject after having been presented a full explanation of the purpose and nature of all the procedures used. The study was approved by the institutional review board of the National Taiwan University Hospital (200611031R).

This study enrolled patients who were referred to the TAIPAI study group and the patients underwent aldosterone-to-renin ratio (ARR) testing for case detection of possible PA during the study period, including 2 medical centers, 3 affiliated hospitals, and 2 regional hospitals in different cities in Taiwan.<sup>25</sup> Patients with other secondary HTN including, renovascular hypertension, Cushing's syndrome, hyperthyroidism, and pheochromocytoma were excluded from this study.<sup>26</sup> Patients were instructed to maintain their usual sodium intake during the study, and adherence was assessed by measuring urinary sodium excretion at each visit. All antihypertensive medications were discontinued for a minimum of 14 days before the screening tests. Doxazosin and/or diltiazem were administered to control markedly high BP when required.<sup>27</sup>

### Diagnosis and further lateralization of PA

The diagnosis of PA was established in hypertensive patients on the basis of the following criteria<sup>17–19,28–30</sup>:

### Confirmation

Fulfillment of the following 3 conditions confirmed a diagnosis of PA:

- (1) autonomous excess aldosterone production evidenced with a 24-h urinary aldosterone level (Uald-24 h) more than 20.3  $\mu\text{g}$ <sup>25</sup>;
- (2) a TAIPAI score larger than 60%<sup>21</sup>; and
- (3) post-SIT aldosterone level >10 ng/dL, or ARR > 35 (ng/dL)/(ng/mL/h) shown in a post-captopril/losartan test, or plasma aldosterone level > 6 ng/dL indicated by a fludrocortisone suppression test.<sup>31</sup>

### Subtype identification

APA is identified on the basis of PA patients according to the following: (1) adrenal adenoma evidenced with a computed tomography (CT) scan for preoperative evaluation; (2) lateralization of aldosterone secretion at adrenal venous sampling or during dexamethasone suppressing NP-59 single-photon emission computed tomography/CT<sup>32</sup>; or (3) pathologically proven adenoma after an adrenalectomy for those who undergo surgery, and subsequent evidence of either a complete or partial cure pattern of hypertension.<sup>15</sup> Idiopathic bilateral hyperplasia is distinguished on the PA patients according to the following: (1) evidence of bilateral diffuse enlargement indicated by a CT scan; (2) nonlateralization of aldosterone secretion at adrenal venous sampling or during dexamethasone suppression NP-59 single-photon emission computed tomography/CT,<sup>32</sup> or (3) evidence of diffuse cell hyperplasia reported in pathology studies for those undergoing operations.

### Functional survey

The aldosterone concentration was measured by radioimmunoassay, using a commercial kit (Aldosterone Maia Kit, Adaltis Italia SPA, Bologna, Italy)<sup>33</sup> and plasma renin activity was measured by the generation of angiotensin I in vitro, using a commercially available radioimmunoassay kit (DiaSorin, Stillwater, MN, USA).<sup>25</sup>

### Clinical parameters

We recorded age, sex, body mass index (BMI), BP, anti-HTN medication, HTN duration, serum creatinine, K, renin-to-aldosterone ratio, 24-hour amount of urine albumin, estimated glomerular filtration rate ([eGFR] calculated using the Chronic Kidney Disease Epidemiology Collaboration formula),<sup>34</sup> renin and aldosterone levels, as well as pre-SIT and post-SIT aldosterone levels.

The data at 1 year after adrenalectomy, including BP, anti-HTN medications, K, and renin and aldosterone levels were examined to evaluate the outcome after adrenalectomy.

### Outcomes

We defined the clinical outcome according to the PASO consensus (Supplemental Table 1): clinical success (complete and partial clinical success) indicating normal BP without anti-HTN medication, the same BP with less anti-HTN medication or a reduction in BP with either the same amount or less anti-HTN medication 1 year after surgery. Resist HTN signifies unchanged or increased BP levels with either the same amount or an increase in anti-HTN medication at 1 year after surgery.

### Statistical analysis

For baseline characteristics, continuous variables were expressed as mean  $\pm$  standard deviation and categorical variables were expressed as frequency and percentage. For continuous variables, the differences among groups were compared using the Mann-Whitney *U* test. For categorical variables, the  $\chi^2$  or Fisher exact test was used. Logistic regression analysis was performed to identify

**Table 1**

Basic characteristics of PA patients with outcome of clinical success and resist HTN after unilateral adrenalectomy

	All patients	Clinical success	Resist HTN	P value
Patient n (%)	236 (100)	188 (79.7)	48 (20.3)	
Age (y)	49.8 ± 11.0	49.7 ± 11.2	50.1 ± 10.3	.915
Male (%)	41.1	39.9	45.8	.455
BMI (kg/m <sup>2</sup> )	25.6 ± 4.3	25.4 ± 4.3	26.3 ± 4.2	.089
DM (%)	13.1	12.8	14.6	.739
Hyperlipidemia	20.8	18.6	29.2	.108
LVH (%)	18.2	17.6	20.8	.599
SBP (mmHg)	155 ± 21	157 ± 22	147 ± 14	.003
DBP (mmHg)	93 ± 15	94 ± 15	90 ± 12	.112
MBP (mmHg)	114 ± 16	115 ± 16	109 ± 11	.017
Hypertension duration (years)	7.4 ± 6.8	7.3 ± 7.0	7.5 ± 6.3	.579
Lowest K (mEq/L)	3.4 ± 0.6	3.3 ± 0.6	3.6 ± 0.6	.005
Cre (mg/dL)	0.9 ± 0.5	0.9 ± 0.5	0.9 ± 0.3	.093
eGFR (mL/min/1.73m <sup>2</sup> )	90.6 ± 22.9	91.3 ± 23.4	87.5 ± 20.8	.118
Albuminuria (g/day)	0.16 ± 0.65	0.18 ± 0.72	0.06 ± 0.14	.173
Renin (ng/L/h)	0.8 ± 3.3	0.7 ± 3.2	1.0 ± 3.6	.021
Aldosterone (ng/dL)	53.7 ± 32.9	56.0 ± 34.2	44.5 ± 25.8	.025
ARR (ng/dL per ng/mL/h)	1247 ± 2363	1425 ± 2521	546 ± 1408	.001
Pre-SIT aldosterone (ng/dL)	60.2 ± 49.8	58.6 ± 38.7	66.7 ± 80.6	.798
Post-SIT aldosterone (ng/dL)	39.1 ± 26.5	40.8 ± 27.9	32.4 ± 19.1	.097

NOTE: All quantitative and normally distributed variables are reported as mean ± standard.

Cre, creatinine; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; LVH, left ventricular hypertrophy; MBP, mean blood pressure; SBP, systolic blood pressure; SIT, saline-infusion test.

determinants of clinical outcome. To determine the variables of significance, we put the variables that were known predictors found by earlier studies or with a *P* value less than .1 in univariate logistic regression analysis into multivariate logistic regression analysis.

A generalized additive model (GAM) was plotted adjusted for sex and age in individual patients.<sup>18,35</sup> The optimal cutoff value was defined as a log odds value of 0.<sup>36</sup> After finding the possible predictors by logistic regression in our database, model discrimination was determined by examining the incremental improvement from the possible predictors with post-SIT aldosterone level to outcome prediction compared with that of a model without post-SIT aldosterone level. Incremental improvement in outcome prediction was determined by examining the change in the area under the receiver operating characteristic curve, the net reclassification index (NRI), and integrated discrimination improvement (IDI).<sup>37</sup> The NRI is a measure of correct reclassification of a new model compared with an old model, and IDI is a measure of the slope for model discrimination between a new and old model.<sup>37–39</sup>

The decision curve analysis graphically is used for the clinical usefulness of each model based on a continuum of potential thresholds for clinical success (x axis) and the net benefit of using the model to clinical success stratify patients (y axis) with a baseline assumption that no patient will achieve success clinical outcome.<sup>40</sup>

We used R software, v 3.4.4 (Free Software Foundation, Inc, Boston, MA, USA<sup>41</sup>) and IBM SPSS statistics v 24 (IBM Corp, Armonk, NY, USA) software. A two-sided *P* value < .05 was considered statistically significant.

## Results

### Baseline characteristics of the study population

A total of 236 PA patients who had undergone adrenalectomy were enrolled in this study. The mean age of all participants was 49.8 ± 11.0 years, and the proportion of men was 41.1%. The mean post-SIT aldosterone level was 39.1 ± 26.5 ng/dL (Table 1).

In our cohort, 79.7% patients achieved clinical success (complete and partial clinical success) after adrenalectomy at 1-year follow-

up. We observed no statistically significant differences in age, gender, or history with diabetes mellitus and left ventricular hypertrophy, eGFR, 24-hour urine albumin excretion, HTN duration, or pre-SIT aldosterone level between the 2 groups. However, the clinical success group had higher systolic BP (157 ± 22 vs 147 ± 14, *P* = .003) and mean BP (115 ± 16 mmHg versus 109 ± 11 mmHg, *P* = .017), lower K (3.3 ± 0.6 mEq/L vs 3.6 ± 0.6 mEq/L, *P* = .005), and renin level (0.7 ± 3.2 ng/L/h versus 1.2 ± 3.7 ng/L/h, *P* = .004) than the resist HTN group. The clinical success group also had relatively lower BMI (25.4 ± 4.3 kg/m<sup>2</sup> vs 26.3 ± 4.2 kg/m<sup>2</sup>, *P* = .089) and higher post-SIT aldosterone level (40.8 ± 27.9 ng/L vs 32.4 ± 19.1 ng/L, *P* = .097 [Table 1]).

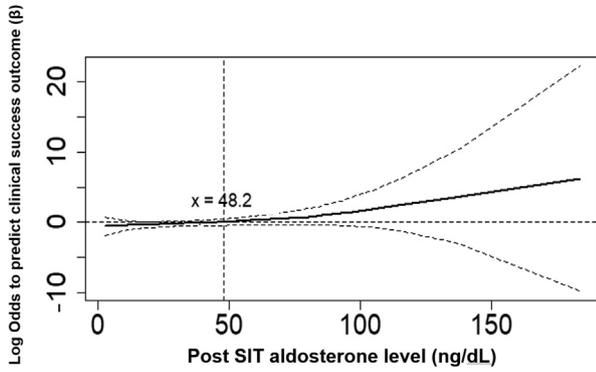
We also analysed the characteristics between higher and lower post-SIT aldosterone level groups (Supplemental Table II). Patients with higher post-SIT aldosterone level (cut point: 48 ng/dL) had higher mean BP (117 ± 18 vs 112 ± 15 mmHg, *P* = .043), higher 24-hour urine albumin excretion (0.24 ± 0.87 vs 0.13 ± 0.53 mg/day, *P* = .017) and lower lowest K level (3.0 ± 0.6 vs 3.5 ± 0.6 mEq/L, *P* < .001).

### Risks forecasting clinical success after adrenalectomy in PA patients

We used the GAM plot to find adequate cut-point values of the continuous parameter to predict clinical success outcome (Fig 1–4). In our cohort, we found that higher post-SIT aldosterone levels (cut point: 48 ng/dL [Fig 1]), higher mean BP (cut point: 115 mmHg [Fig 2]), lower lowest K levels (cut point: 3.2 mEq/L [Fig 3]), and lower BMI (cut point: 25 kg/m<sup>2</sup> [Fig 4]) had higher clinical success rates.

Post-SIT aldosterone levels higher than 48 ng/dL (odds ratio [OR] = 2.42; 95% confidence interval [CI], 1.02–4.73; *P* = .044), mean BP higher than 115 mmHg (OR = 2.43; 95% CI, 1.22–4.82; *P* = .011), and lowest K level less than 3.2 mEq/L (OR = 2.08; 95% CI, 1.02–4.25; *P* = .045) could predict clinical success after adrenalectomy. BMI lower than 25 kg/m<sup>2</sup> (OR = 1.74; 95% CI, 0.91–3.33; *P* = .095) and renin higher than 1 ug/L/h (OR = 2.21; 95% CI, 0.96–5.10; *P* = .063) had a higher clinical success rate without statistical significance (.05 < *P* < .1 [Table II]).

In multivariate logistic regression analysis (Table II), post-SIT aldosterone levels higher than 48 ng/dL (OR = 2.51; 95% CI,

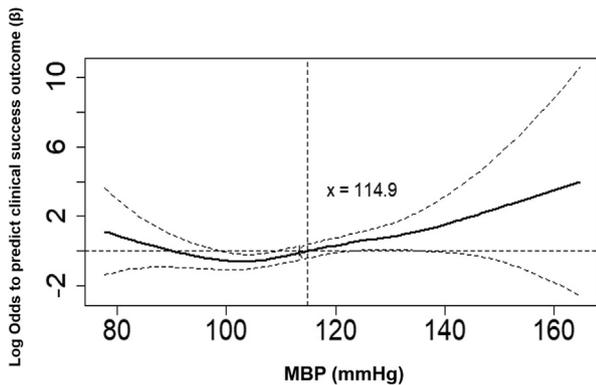


**Fig 1.** GAM plot for the association between post-SIT aldosterone level and clinical success outcome. Optimal post-SIT aldosterone level cut-point value (48 ng/dL) suggested by the GAM plot. The association is between post-SIT aldosterone level and the odds ratio for clinical success outcome and is adjusted simultaneously by age and gender. The X axis is post-SIT aldosterone concentration. The Y axis is log odds to clinical success. Dotted curves indicate 95% CIs for the smoothed hazard. GAM, generalized additive model; SIT, saline-infusion test.

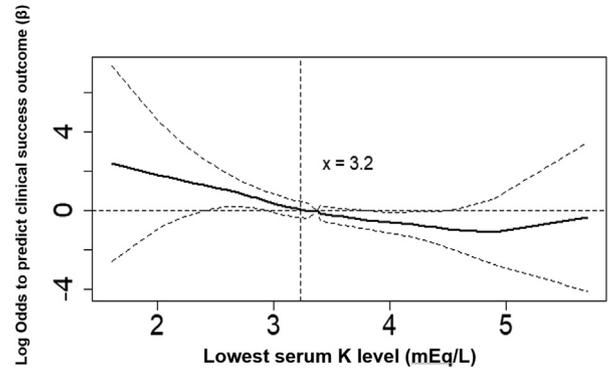
1.04–6.06;  $P = .040$ ), BMI less than 25 kg/m<sup>2</sup> (OR = 2.22; 95% CI, 1.12–4.40;  $P = .023$ ), and mean BP higher than 115 mmHg (OR = 2.79; 95% CI, 1.37–5.68;  $P = .005$ ) were independently predictive of clinical success.

*Incremental benefit prediction of post-SIT aldosterone level from traditional clinical predictors*

In multivariate logistic regression analysis, we found that post-SIT aldosterone, BMI, and mean BP could predict clinical success independently. Therefore, we used these predictors to estimate the additional benefit from post-SIT aldosterone on clinical outcome prediction. Incremental improvements to clinical success outcome provided by post-SIT aldosterone levels higher than 48 ng/dL compared with known clinical predictors (mean BP higher than 115 mmHg and BMI) were also found in our cohort. The variables were determined by the multivariable logistic regression analysis with statistical significance. For outcomes of clinical success, compared with mean BP higher than 115 mmHg and BMI derived from clinical predictors, the addition of post-SIT aldosterone level increased the area under the receiver operating characteristic curve from 0.645 (95% CI, 0.561–0.728;  $P = .002$ ) to 0.685 (95% CI, 0.602–0.768;  $P <$



**Fig 2.** GAM plot for the association between MBP and clinical success outcome. Optimal MBP cut-point value suggested by GAM plot. The association is between MBP (115 mmHg) and the odds ratio for clinical success outcome and is adjusted simultaneously by age and gender. The X axis is MBP. The Y axis is log odds to clinical success. Dotted curves indicate 95% CIs for the smoothed hazard. GAM, generalized additive model; MBP, mean blood pressure.



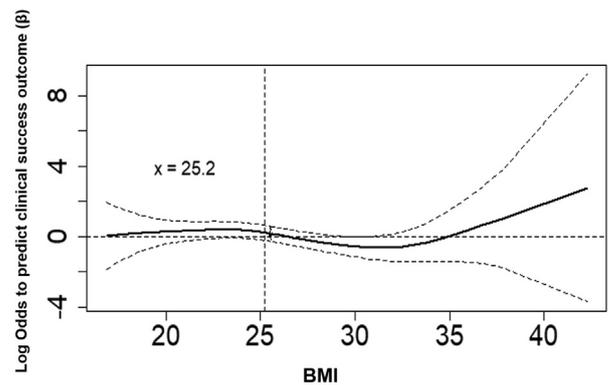
**Fig 3.** GAM plot for the association between lowest K level and clinical success outcome. Optimal lowest K level cut-point value (3.2 mEq/L) suggested by GAM plot. The association is between the lowest K level and the odds ratio for clinical success outcome and is adjusted simultaneously by age and sex. The X axis is the lowest K level. The Y axis is log odds to clinical success. Dotted curves indicate 95% CIs for the smoothed hazard. GAM, generalized additive model; K, potassium.

.001 [Table III]). The NRI was 0.293 (95% CI, 0.055–0.532;  $P = .016$ ) and the IDI was 0.016 (95% CI, 0.004–0.03;  $P = .049$  [Table III]). Discrimination (based on the C statistic and the IDI) was higher when the known clinical predictors were added with post-SIT aldosterone levels.

Finally, decision curve analysis was plotted to assess the clinical success after adrenalectomy, using post-SIT aldosterone in addition to BMI and mean BP (Fig 5). Net benefit is the net proportion of patients who could benefit from the offered predicting model. For risk thresholds more than 66%, the forecasting strategy is better when utilizing the clinical success score together with post-SIT aldosterone. For moderate-risk to high-risk thresholds (0%–66%), using clinical success predicting score with post-SIT aldosterone level was similar to the clinical score (BMI and mean BP).

**Discussion**

This is the first large cohort study to evaluate post-SIT aldosterone levels based on the prediction of outcome of clinical success as defined by PASO consensus in PA patients after adrenalectomy. In this observational cohort study, we demonstrated that the post-SIT aldosterone level was not only a physiologic response but could also be a predictor of clinical success in PA patients after



**Fig 4.** GAM plot for the association between BMI and clinical success outcome. Optimal BMI cut-point value (25 kg/m<sup>2</sup>) suggested by GAM plot. The association is between BMI and the odds ratio for clinical success outcome and is adjusted simultaneously by age and gender. The X axis is BMI. Y axis is log odds to clinical success. Dotted curves indicate 95% CIs for the smoothed hazard. GAM, generalized additive model; BMI, body mass index.

**Table II**  
Baseline correlates of clinical success (complete clinical and partial clinical success) after unilateral adrenalectomy in PA patients

	Univariate		Multivariate	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Post-SIT aldosterone >48 ng/dL	2.42 (1.02–5.73)	.044	2.51 (1.04–6.06)	.040
Age, per year	0.99 (0.97–1.03)	.836		
Sex, male	1.28 (0.67–2.41)	.456		
BMI <25 kg/m <sup>2</sup>	1.74 (0.91–3.33)	.095	2.22 (1.12–4.40)	.023
Mean BP >115mmHg	2.43 (1.22–4.82)	.011	2.79 (1.37–5.68)	.005
K <3.2mEq/L	2.08 (1.02–4.25)	.045		
eGFR, (mL/min/1.73m <sup>2</sup> )	1.01 (0.99–1.02)	.302		
Hypertension duration (year)	0.99 (0.95–1.04)	.878		
Renin >1 ug/L/h	2.21 (0.96–5.10)	.063		

NOTE: Analysis by univariate and multivariate logistic regression. eGFR, estimated glomerular filtration rate; SIT, saline-infusion test.

**Table III**  
Comparison of model discrimination between the model integration with post-SIT aldosterone level for clinical success prediction in PA patients after unilateral adrenalectomy

Model performance	MBP > 115 BMI	Post-SIT aldo > 48 MBP > 115 BMI
C statistic (95% CI)	0.645 (0.561–0.728)	0.685 (0.602–0.768)
P value for C statistic	.002	< .001
NRI (95% CI)	—	0.293 (0.055–0.532)
P value for NRI	—	.016
IDI (95% CI)	—	0.016 (0.004–0.03)
P value for IDI	—	.049

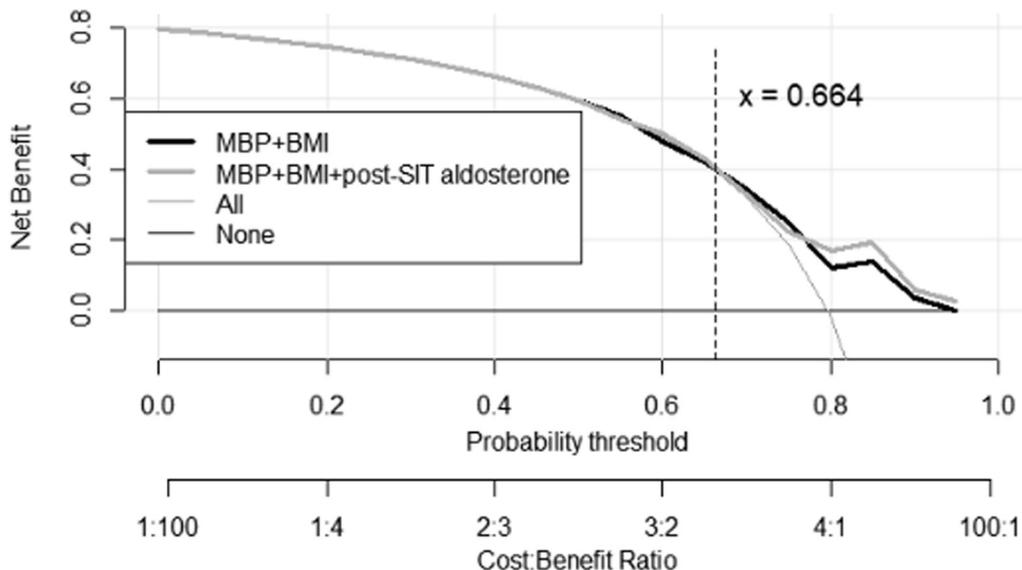
AUC, area under the receiver operating characteristic curve; MBP, mean blood pressure; SIT, saline-infusion test.

adrenalectomy. In addition, our study revealed that BMI lower than 25 kg/m<sup>2</sup> and mean BP higher than 115 mmHg could also forecast outcomes.

*The role of post-SIT aldosterone level*

SIT is validated to be a reasonable and convenient confirmatory test of PA, showing a specificity of 84% and sensitivity of 88%, with a cutoff value of 5 ng/dL.<sup>42</sup> Currently, SIT is the most widely used confirmatory test for PA diagnosis in many countries.

We found the additional benefit of SIT on prediction of the clinical outcome after adrenalectomy. In 2015, Weigel et al<sup>16</sup> demonstrated that a higher post-SIT aldosterone level was associated with a higher BP and a lower K level before targeted treatment and a higher remission rate after adrenalectomy. However, their study included a limited number of APA patients and some non-APA patients who may have received less benefit from surgery. In our study, PA patients with higher post-SIT aldosterone levels could benefit more from adrenalectomy according to the newly defined PASO criteria. According to our decision curve analysis, post- SIT



**Fig 5.** Decision curve analysis for the post-SIT aldosterone plus model 1 (MBP and BMI) and model 1 (MBP and BMI) predicting clinical success outcome prediction models. BMI, body mass index; MBP, mean blood pressure; SIT, saline-infusion test.

aldosterone is an independent factor that could add the performance of the forecasting model.

The post-SIT aldosterone level could not be suppressed in PA patients, however, a few reports demonstrated the association between high post-SIT aldosterone levels and disease characteristics. Our finding suggests that PA patients have a better clinical outcome, in part, via restoration of higher post-SIT aldosterone level, higher mean BP, higher 24-h urine albumin excretion, and lower lowest K (Supplemental Table II).

Wide variations have been reported in clinical remission rates (16%–72%) among various studies. Earlier studies have also reported the outcome of adrenalectomy for PA but divergent and ill-defined criteria with varied follow-up intervals have been employed to assess outcome.<sup>43–47</sup> Outcome results vary widely across studies and may underestimate or overestimate the outcome effects defined by PASO criteria.

The renin–angiotensin–aldosterone system plays an important role in vascular stiffening, which was associated with BP.<sup>48,49</sup> Specifically, the mineralocorticoid hormone, aldosterone, will contribute to arterial stiffness both in human patients and in experimental models.<sup>50,51</sup> In light of an earlier study,<sup>16</sup> our results have shown that patients who have higher post-SIT aldosterone have lower serum K, higher proteinuria, and higher BP, relatively suffering more severe conditions than their counterparts. Taken together, the PA patients who could benefit from BP control from adrenalectomy were those who had high disease severity.

#### Higher mean BP and lower BMI gained more benefit in PA patients after adrenalectomy

In our cohort, we found that higher mean BP and lower BMI had a higher clinical success rate after adrenalectomy. The patients with higher mean BP may represent refractory to anti-HTN medications control. Adrenalectomy may give more benefit to refractory BP patients.

Other studies have demonstrated a significant positive correlation between BMI, fat percentage, and BP (both systolic as well as diastolic BP).<sup>52,53</sup> Adipocyte dysfunction and obesity contribute to hypertension via the endocrine and paracrine effects of adipose tissues-derived adipokines on vascular endothelial cells, vascular smooth muscle cells, and inflammatory cells, including macrophages.<sup>54–57</sup> This association decreased the benefit from adrenalectomy in PA patients with higher BMI.

Our study has several limitations. First, we did not evaluate races, gene mutation (eg, KCNJ5 mutation), and tumor size as variables in our cohort. Although our study found several predictors of clinical outcome after adrenalectomy, the cutoff values of the variables may not be applicable to various races, and further investigations are needed. Second, the sample size in our study is relatively small. To resolve this, we used a series statistical analysis and obtained consistent results. The third limitation is the lack of an ambulatory BP record at baseline and postsurgery to provide a more standardised assessment of BP response to adrenalectomy. However, official BP is used for real-world practice and can be a proxy for hypertensive status.

In conclusion, our study showed that the post-SIT aldosterone level is not only a physiologic response for confirmation but also could forecast clinical outcome after adrenalectomy in PA patients. In addition, our study also revealed the benefit of identifying BMI lower than 25 kg/m<sup>2</sup> and mean BP higher than 115 mmHg on the prediction clinical success. Further investigation is necessary to identify the PA patients who could gain more benefit from adrenalectomy according to the newly clinical outcome criteria by the PASO consensus.

## Acknowledgments

We thank the staff of Biotechnology R&D Center, National Taiwan University Hospital, Hsin-Chu Branch, for their assistance in the statistical analysis.

## Conflict of interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.surg.2019.05.001>.

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