Clinical risk factors of postoperative hyperkalemia after adrenalectomy in patients with aldosterone-producing adenoma

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Abstract

Objective: Unilateral adrenalectomy is the first-line treatment for aldosterone-producing adenomas (APAs). Hyperkalemia after adrenalectomy because of contralateral zona glomerulosa insufficiency has been reported. We investigated clinical risk factors to predict postoperative hyperkalemia in patients with APA undergoing adrenalectomy.

Design and methods: This study was conducted by retrospectively reviewing medical records from 2000 to 2012 at Seoul National University Hospital and two other tertiary centers. Data from 124 patients who underwent adrenalectomy were included. Hyperkalemia was defined as serum potassium >5.5 mmol/l. Clinical preoperative risk factors included age, blood pressure, plasma renin activity (PRA), plasma aldosterone concentration (PAC), serum potassium, serum creatinine, glomerular filtration rate (GFR), the mass size on pathology, and mineralocorticoid receptor (MR) antagonist use.

Results: Out of 124 patients, 13 (10.5%) developed postoperative hyperkalemia. The incidences of transient and persistent hyperkalemia were 3.2 and 7.3% respectively. Preoperative PRA and PAC were not significantly different in postoperative hyperkalemic patients compared with normokalemic patients. Patients with persistent hyperkalemia were older, had a longer duration of hypertension, larger mass size on pathology, and lower GFR (all P<0.05). The incidence of postoperative hyperkalemia was not different between MR antagonist users and non-users.

Conclusion: Older age (≥53 years), longer duration of hypertension (≥9.5 years), larger mass size on pathology (≥1.95 cm), and impaired preoperative renal function (GFR <58.2 ml/min) were associated with prolonged postoperative hyperkalemia in patients with APA. MR antagonist use did not prevent postoperative hyperkalemia.

Introduction

Primary aldosteronism (PA) is an excess of aldosterone secretion from the adrenal glands. The prevalence of PA is reported to be between 5 and 20% in patients with hypertension (1). Abnormally high production of aldosterone causes hypertension and hypokalemia, both of which lead to cardiovascular and renal complications.

Unilateral adrenalectomy is the curative treatment for aldosterone-producing adenomas (APAs) (2). Postoperative hyperkalemia and renal insufficiency have been reported previously, although the incidence is low (3, 4). The reasons for prolonged selective suppression of aldosterone secretion after unilateral adrenalectomy...
remain unclear. Although prolonged postoperative hyperkalemia has been reported in relation to underlying chronic kidney disease, long duration of hypertension, and severe PA (5, 6), the cut-off values of aforementioned variables have not been evaluated because of the low incidence of postoperative hyperkalemia.

Moreover, the association between the use of mineralocorticoid receptor (MR) antagonists such as spironolactone and the development of postoperative hyperkalemia is controversial. Some researchers advocate the use of MR antagonists for 2–4 weeks before surgery to control hypertension and hypokalemia (2, 7). This is because MR antagonists may prevent mineralocorticoid deficiency after adrenalectomy by desensitizing MRs (8, 9). Another mechanism by which preoperative MR antagonists may prevent aldosterone deficiency postoperatively is ‘unsuppression’ of renin/angiotensin leading to stimulation of aldosterone production by the contralateral gland. On the other hand, long-duration treatment with MR antagonists may aggravate postoperative hyperkalemia by antagonizing MRs (10). A recent study in Germany has found a similar incidence of postoperative hyperkalemia between preoperative MR antagonist users and non-users (6).

The aim of this study was to estimate the incidence of postoperative hyperkalemia and the clinical risk factors predicting postoperative hyperkalemia in patients with APA. We also assessed the effect of MR antagonists on the development of postoperative hyperkalemia.

**Patients and methods**

**Study subjects**

This study was conducted by retrospectively reviewing medical records from Seoul National University Hospital (n=69), Seoul National University Bundang Hospital (n=45), and Boramae Medical Center (n=10) from 2000 to 2012. A total of 124 patients who had been followed up for at least 3 months after adrenalectomy were included in the final analysis.

The saline infusion test was performed to confirm PA in patients with hypertension and an elevated aldosterone-to-renin ratio (2). We conducted adrenal venous sampling used to lateralize APA in all three hospitals (11). A cut-off of the cortisol-corrected aldosterone ratio from high side to low side more than 4:1 and from low side to inferior vena cava of <1.0 was used to indicate unilateral aldosterone excess. We confirmed APA by the identification of adrenal adenoma at pathological tissues and demonstration of correction of the hyperaldosteronism and cure, or marked improvement of the hypertension after adrenalectomy (12). Before confirming diagnosis, previously used antihypertensive medications were changed to calcium channel blockers or α-adrenergic receptors, which do not interfere with the renin–angiotensin–aldosterone system. After surgery, none of the patients took any ACE inhibitors, angiotensin II receptor blockers, or non-steroidal anti-inflammatory drugs.

The majority of the patients (74.2%) were treated with an MR antagonist (spironolactone) until the day before surgery. The decision to give an MR antagonist was made by the ordering physicians. The MR antagonist and potassium supplementation were discontinued immediately following surgery. The patients used their usual antihypertensive medication until their first postoperative visit. Postoperatively, patients were educated to take a low-potassium diet to avoid postoperative hyperkalemia.

This study was approved by the institutional review board of Seoul National University Hospital and was conducted according to the Declaration of Helsinki.

**Laboratory and preoperative clinical parameters**

Hyperkalemia was defined as serum potassium >5.5 mmol/l. Transient postoperative hyperkalemia was defined as hyperkalemia that occurred within the first 3 months after surgery and resolved spontaneously after 3 months. Persistent postoperative hyperkalemia was defined as hyperkalemia that continued more than 3 months after surgery.

Clinical risk factors such as age, sex, blood pressure (BP), duration of hypertension, plasma renin activity (PRA), plasma aldosterone concentration (PAC), serum potassium, serum creatinine, glomerular filtration rate (GFR), the size of the APA, and use of an MR antagonist were included. All variables were retrieved from our medical records. Blood samples were drawn in a fasting state using a tourniquet as quickly as possible. Initial BP was measured at the first outpatient clinic visit. Postoperative BP was measured 1 month after the operation at the first postoperative outpatient clinic visit. PRA was measured using the Renin RIA beads (TFB, Inc., Tokyo, Japan) before 2011 and using a PRA RIA kit (TFB, Inc.) after 2011. The intra- and inter-assay coefficient of variation (CV) values were 3.8 and 6.7% respectively. PAC was determined by RIA using the SPAC-S aldosterone kit (TFB, Inc.). The intra- and inter-assay CV values were 4.7 and 4.5% respectively. We measured the adenoma size on pathological tissue specimens.

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Statistical analyses

Data are expressed as mean ± s.d. or median (25th percentile, 75th percentile) or n (%). ANOVA (parametric data), Kruskal–Wallis (non-parametric data), and χ² tests were used to compare continuous and categorical variables respectively. Post-hoc analysis was performed using the Bonferroni method. Using receiver operating characteristic (ROC) curve analysis, we estimated the cut-off points for parameters such as age, duration of hypertension, mass size on pathology, and preoperative estimated GFR values. Risk factors for postoperative persistent hyperkalemia were included in multivariate logistic regression analyses. Statistical analysis was performed using SPSS version 18 (IBM, SPSS, Inc.). P < 0.05 was considered statistically significant.

Results

In a total of 124 patients, postoperative transient hyperkalemia occurred in four and persistent hyperkalemia in nine. Seven patients had severe hyperkalemia (>6.0 mmol/l) at 1 month postoperatively and five patients at 3 months postoperatively. Ninety-two percent of patients (n = 114) presented with hypokalemia (<3.5 mmol/l) at diagnosis of PA.

The clinical and laboratory characteristics of patients with normokalemia, transient hyperkalemia, and persistent hyperkalemia postoperatively are shown in Table 1. Patients in the group with persistent hyperkalemia were older and had a longer duration of hypertension than those in the groups with normokalemia or transient hyperkalemia. Moreover, subjects in the persistent hyperkalemia group showed significantly higher serum creatinine levels and lower GFR levels compared with those in the other groups preoperatively. The adenoma size confirmed by a pathologist was largest in patients with persistent hyperkalemia compared with those in the other two groups. There was no difference in preoperative BP, lowest serum potassium level, PRA, PAC, and ARR between

Table 1 Clinical and laboratory parameters of patients according to postoperative potassium levels. Data are expressed as mean ± s.d. or median (25th, 75th percentile).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Postoperative normokalemia (n = 111)</th>
<th>Postoperative transient hyperkalemia (n = 4)</th>
<th>Postoperative persistent hyperkalemia (n = 9)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset age (years)</td>
<td>46.1 ± 11.0</td>
<td>48.5 ± 12.4</td>
<td>57.2 ± 6.6</td>
<td>0.014</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>52/62</td>
<td>0/4</td>
<td>6/3</td>
<td>0.160</td>
</tr>
<tr>
<td>Follow-up period (years)</td>
<td>3.3 ± 2.6</td>
<td>2.8 ± 2.1</td>
<td>2.3 ± 2.1</td>
<td>0.522</td>
</tr>
<tr>
<td>Duration of hypertension (years)</td>
<td>3.0 (0.0–7.0)</td>
<td>7.0 (0.3–14.5)</td>
<td>10.0 (8.5–22.0)</td>
<td>0.014</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>5.3% (n = 6)</td>
<td>0% (n = 0)</td>
<td>11.1% (n = 1)</td>
<td>0.674</td>
</tr>
<tr>
<td>Preoperative SBP (mmHg)</td>
<td>157.3 ± 23.0</td>
<td>140.5 ± 33.2</td>
<td>159.6 ± 10.9</td>
<td>0.329</td>
</tr>
<tr>
<td>Preoperative DBP (mmHg)</td>
<td>97.1 ± 15.8</td>
<td>87.8 ± 26.1</td>
<td>96.1 ± 11.9</td>
<td>0.508</td>
</tr>
<tr>
<td>Preoperative PRA (ng/ml per h)</td>
<td>0.10 (0.10, 0.29)</td>
<td>0.15 (0.10, 0.73)</td>
<td>0.10 (0.10, 0.10)</td>
<td>0.307</td>
</tr>
<tr>
<td>Preoperative PAC (ng/dl)</td>
<td>34.9 (23.8, 50.7)</td>
<td>40.3 (32.9, 46.2)</td>
<td>41.7 (25.8, 109.3)</td>
<td>0.493</td>
</tr>
<tr>
<td>Preoperative ARR</td>
<td>247 (86, 465)</td>
<td>265.8 (84.8, 432)</td>
<td>417 (258, 641)</td>
<td>0.151</td>
</tr>
<tr>
<td>Preoperative creatinine (mg/dl)</td>
<td>0.91 ± 0.23</td>
<td>0.73 ± 0.20</td>
<td>1.34 ± 0.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Preoperative GFR (ml/min)</td>
<td>83.3 ± 21.8</td>
<td>96.0 ± 37.1</td>
<td>53.1 ± 23.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Preoperative lowest K (mmol/l)</td>
<td>2.81 ± 0.51</td>
<td>2.80 ± 0.18</td>
<td>2.88 ± 0.69</td>
<td>0.091</td>
</tr>
<tr>
<td>Preoperative hypokalemia (%)</td>
<td>102 (91.9)</td>
<td>4 (100.0)</td>
<td>8 (88.9)</td>
<td>0.793</td>
</tr>
<tr>
<td>Preoperative number of antihypertensives</td>
<td>1.00 (1.00, 3.00)</td>
<td>2.00 (1.00, 2.25)</td>
<td>2.00 (1.00, 3.50)</td>
<td>0.706</td>
</tr>
<tr>
<td>Preoperative MR antagonist (%)</td>
<td>84 (75.7)</td>
<td>3 (75.0)</td>
<td>6 (66.7)</td>
<td>0.835</td>
</tr>
<tr>
<td>Mass on pathology (cm)</td>
<td>1.60 ± 0.58</td>
<td>1.75 ± 0.33</td>
<td>2.22 ± 0.94</td>
<td>0.014</td>
</tr>
<tr>
<td>Postoperative SBP (mmHg)</td>
<td>126.7 ± 14.9</td>
<td>112.3 ± 16.5</td>
<td>121.9 ± 8.5</td>
<td>0.110</td>
</tr>
<tr>
<td>Postoperative DBP (mmHg)</td>
<td>83.2 ± 9.6</td>
<td>69.8 ± 10.1</td>
<td>81.2 ± 10.1</td>
<td>0.025</td>
</tr>
<tr>
<td>Postoperative PRA (ng/ml/h)*</td>
<td>1.40 (0.60, 2.60)*</td>
<td>1.50 (0.40, 1.50)*</td>
<td>1.10 (0.12, 25.10)*</td>
<td>0.954</td>
</tr>
<tr>
<td>Postoperative PAC (ng/dl)*</td>
<td>9.3 (6.3, 12.3)*</td>
<td>8.4 (6.7, 8.4)*</td>
<td>5.5 (4.5, 8.7)*</td>
<td>0.137</td>
</tr>
<tr>
<td>Postoperative ARR</td>
<td>63.0 (30.0, 15.0)</td>
<td>5.6 (3.4, 5.6)</td>
<td>7.5 (1.4, 29.9)</td>
<td>0.966</td>
</tr>
<tr>
<td>Postoperative creatinine (mg/dl)**</td>
<td>1.00 ± 0.31*</td>
<td>1.22 ± 0.38*</td>
<td>1.70 ± 0.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative GFR (ml/min)**</td>
<td>76.9 ± 23.0</td>
<td>53.3 ± 16.8*</td>
<td>39.8 ± 26.0*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative number of antihypertensives</td>
<td>0.00 (0.00, 1.00)</td>
<td>0.00 (0.00, 1.00)</td>
<td>1.00 (0.00, 2.00)</td>
<td>0.136</td>
</tr>
</tbody>
</table>

OP: operative/operator; ant, antagonist; SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate; PAC, plasma aldosterone concentration; PRA, plasma renin activity; MR, mineralocorticoid receptor.

*P < 0.05 vs preoperative values.
the three groups. The use of an MR antagonist was not related to the risk of developing postoperative hyperkalemia. PAC decreased and PRA increased in all three groups after adrenalectomy. Postoperatively, subjects in the group with persistent hyperkalemia had higher serum creatinine and lower GFR levels than the other groups.

We performed ROC analysis to determine the cut-off points for each parameter related to persistent postoperative hyperkalemia (Fig. 1). The cut-off points for onset age, duration of hypertension, mass size on pathology, and estimated GFR were 53 years, 9.5 years, 1.95 cm, and 58.2 ml/min respectively. We used these cut-off points to predict persistent postoperative hyperkalemia using logistic regression analyses (Table 2). Subjects aged ≥53 years had greater odds (OR=15.6) of developing postoperative hyperkalemia than those aged <53 years. The risk for subjects with hypertension for ≥9.5 years was ten times higher than that for subjects with hypertension for <9.5 years in the age-adjusted model. The OR of a mass size on pathology ≥1.95 cm was 5.78 after adjusting for age. An estimated GFR of <58.2 ml/min was also associated with an increased risk of postoperative hyperkalemia (OR=26.6, P<0.05).

Out of 124 patients, 93 (75.0%) were treated with spironolactone at a mean daily dose of 88 mg for a mean treatment time of 45 days; 41 patients had received the medication for over 1 month. The proportion of MR antagonist users was not significantly different between subjects with postoperative transient hyperkalemia, persistent hyperkalemia, and normokalemia, and the dose and duration of MR antagonist treatment were not significantly different between the groups. Age, creatinine, preoperative serum potassium, PAC, PRA, and BP did not differ between MR antagonist users and non-users. MR antagonist users had better controlled serum potassium levels than MR antagonist non-users based on their preoperative 1-day potassium levels (Table 3).

**Discussion**

In this study, we found that the incidence of post-adrenalectomy hyperkalemia in 124 patients with APA was 10.5%. Moreover, 7.3% of total patients showed persistent postoperative hyperkalemia. In a previous study, the incidence rates of post-adrenalectomy hyperkalemia and prolonged hyperkalemia were 16 and 5% respectively, which is very similar to our findings (6). Another report showed that the incidence of hyperkalemia after adrenalectomy was ~29.1% in patients with APA, but only 5.4% of patients experienced persistent hyperkalemia (12). Unilateral aldosterone excess may suppress contralateral aldosterone production via reduced PRA or lack of response in the contralateral adrenal gland. As circulating aldosterone levels markedly decrease after removal of adenomas, patients are under the risk of developing hyperkalemia. Contrary to adrenal Cushing’s syndrome, the incidence of mineralocorticoid deficiency after adrenalectomy was low. This may be attributed to the relatively fast recovery rate of the zona glomerulosa in the contralateral adrenal gland (13).

**Table 2** Logistic regression models predicting postoperative hyperkalemia in APA patients.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Unadjusted OR (95% CI)</th>
<th>Age-adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥53 years</td>
<td>15.6 (1.9–129)</td>
<td>10.5 (1.86–59.1)</td>
</tr>
<tr>
<td>Duration of hypertension &gt; 9.5 years</td>
<td>17.5 (3.37–90.8)</td>
<td>-</td>
</tr>
<tr>
<td>Mass size on pathology ≥1.95 cm</td>
<td>5.59 (1.31–23.8)</td>
<td>5.78 (1.25–26.8)</td>
</tr>
<tr>
<td>Estimated GFR &lt;58.2 ml/min</td>
<td>45.4 (7.7–267.7)</td>
<td>26.6 (4.10–173)</td>
</tr>
</tbody>
</table>

OR, odds ratio; GFR, glomerular filtration rate.
We investigated clinical risk factors and the associated cut-off values that may predict development of postoperative hyperkalemia. We showed that individuals aged ≥53 years with a longer duration of hypertension ≥9.5 years, mass size on pathology ≥1.95 cm, and impaired renal function (as assessed by estimated GFR <58.2 ml/min) had an increased risk of postoperative persistent hyperkalemia. In this study, age and duration of hypertension were associated with postoperative hyperkalemia. These findings are consistent with those of previous studies (6, 12) and suggest that age and disease duration may contribute to renal insufficiency, leading to postoperative hyperkalemia. We can postulate that a long duration of aldosterone excess could cause a detrimental and irreversible effect on renal damage, which is masked by volume expansion because of hyperaldosteronism. These results are in line with a previous report that small adenoma size (<2 cm) and duration of hypertension ≤6 years are favorable prognostic factors to resolve hypertension after adrenalectomy in APA (14). Postoperative serum potassium levels at 3 months were positively correlated with the duration of hypertension (r=0.237, P=0.003), preoperative PAC levels (r=0.197, P=0.028), and adenoma size on pathology (r=0.332, P<0.001) in our study (data not shown). A previous study has reported that adenoma size was positively correlated with preoperative PAC levels (15). In Table 1, preoperative PAC levels tended to be elevated in patients with persistent postoperative hyperkalemia, but the difference was not statistically significant. Nonetheless, adenoma size on pathology was positively correlated with preoperative PAC levels (r=0.319, P<0.001) (data not shown). In this study, that association between postoperative persistent hyperkalemia and large adenomas may be the consequence of patients with larger adenomas having elevated preoperative PAC levels. Although severe hypokalemia may be related to the duration and/or severity of PA (16), we failed to find a significant relationship among these factors.

In this study, GFR was significantly decreased after adrenalectomy in patients with postoperative hyperkalemia according to decreased PAC. A previous retrospective study has also demonstrated a close relationship between altered renal function and postoperative hyperkalemia (6). Chiang et al. (12) has recently described that duration of hypertension and estimated GFR are independent risk factors associated with post-adrenalectomy hyperkalemia (17). MRs exist in the distal convoluted tubule of the kidney, and aldosterone increases sodium reabsorption via activation of the apical epithelial sodium channel and the basolateral Na+/K+-ATPase (17, 18). Accordingly, the overproduction of aldosterone alters renal sodium and potassium handling and induces inflammation, fibrosis, mesangial cell proliferation, and podocyte injury in the kidney (18). Aldosterone excess leads to vasodilation in afferent and efferent arterioles, contributing to glomerular hyperfiltration in untreated patients (19, 20). Hence, hypoaldosteronism after adrenalectomy increases serum creatinine and reduces GFR, which may lead to marked decreases in salt and water delivery, as well as reduced potassium secretion in the distal region (21).

MR antagonists are usually administered preoperatively to control hypokalemia by restoring the responsiveness of the chronically suppressed renin–angiotensin–aldosterone system. Reversal of hyperaldosteronism after long-term MR antagonist treatment has been reported, as spironolactone has a direct inhibitory effect on adrenal steroidogenesis (9, 22). However, MR antagonist use did not influence the incidence of hyperkalemia in this study. Age, preoperative serum potassium level, BP, kidney function, PAC, and PRA were not different between MR antagonist users and non-users. The duration and cumulative dose of MR antagonists were not significantly different between normokalemic and hyperkalemic patients in this study (data not shown). This may be because the degree and/or

### Table 3  Initial clinical and laboratory parameters between MR antagonist users and non-users. Data are expressed as mean±s.d. or median (25th, 75th percentile).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MR antagonist user (n=33)</th>
<th>MR antagonist non-user (n=31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.6±11.6</td>
<td>51.1±11.6</td>
<td>0.296</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>158.0±23.1</td>
<td>155.2±21.6</td>
<td>0.555</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>98.6±16.3</td>
<td>92.1±13.9</td>
<td>0.047</td>
</tr>
<tr>
<td>Preoperative creatinine (mg/dl)</td>
<td>0.94±0.23</td>
<td>0.90±0.42</td>
<td>0.608</td>
</tr>
<tr>
<td>Preoperative GFR (ml/min)</td>
<td>81.0±21.7</td>
<td>82.3±27.2</td>
<td>0.784</td>
</tr>
<tr>
<td>Preoperative K (mmol/l)</td>
<td>2.78±0.50</td>
<td>2.88±0.56</td>
<td>0.343</td>
</tr>
<tr>
<td>Preoperative 1-day K (mmol/l)</td>
<td>4.11±0.50</td>
<td>3.73±0.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Preoperative PRA (ng/ml per h)</td>
<td>0.10 (0.10, 0.30)</td>
<td>0.10 (0.10, 0.20)</td>
<td>0.224</td>
</tr>
<tr>
<td>Preoperative PAC (ng/dl)</td>
<td>37.0 (27.2, 51.9)</td>
<td>30.6 (17.0, 48.3)</td>
<td>0.140</td>
</tr>
<tr>
<td>Postoperative hyperkalemia (%)</td>
<td>6 (6.5)</td>
<td>3 (9.4)</td>
<td>0.693</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate; PAC, plasma aldosterone concentration; PRA, plasma renin activity; MR, mineralocorticoid receptor.
duration of MR antagonist treatment in our study were not sufficient to restore the contralateral zona glomerulosa (9, 22). MR antagonists may cause prolonged hypoadosteronism because of their long half-life. Further study is needed to determine the optimal dose and duration of MR antagonists to prevent post-adrenalectomy hyperkalemia.

Our study has several limitations. The data were reviewed retrospectively and the timing of the laboratory tests varied between patients. Notably, postoperative PAC levels in some patients with postoperative transient hyperkalemia or normokalemia were unexpectedly high. The reason for this is not clear. However, the timing of PAC and PRA measurement was much varied owing to the retrospective design (range, 7–224 days). Therefore, postoperative PAC and PRA values were not informative in our study. Nevertheless, we collected data according to standard protocols as far as possible, and all three centers in this study used the same methods to measure biochemical parameters such as PAC, PRA, potassium, and creatinine, and diagnostic procedures. The level of serum potassium tends to be higher than that of plasma potassium, because K⁺ is released from the clot, and this may contribute to the apparently high proportion of patients deemed to be hyperkaemic. The decision for spironolactone use was made by the physician, which may introduce a selection bias. However, subject characteristics between MR antagonist users and non-users were not significantly different.

Despite several limitations, our study had some notable strengths. The number of study subjects was relatively large over a relatively long period, and subjects were taken from three centers in Korea. We included only patients who had a postoperative serum potassium level at 3 months. We re-evaluated the benefit of MR antagonists to prevent postoperative hyperkalemia. While the preoperative MR antagonist was useful in the past when only severe typical hypokalemic hyperaldosteronism was diagnosed, it is not essential nowadays when mild-to-moderate normokalemic hyperaldosteronism is also detected.

Taken together, we observed that postoperative persistent hyperkalemia occurred in 7.3% of adrenalectomized patients with unilateral aldosterone excess. Subjects aged ≥53 years with a duration of hypertension ≥9.5 years, mass size on pathology ≥1.95 cm, or GFR ≤58.2 ml/min had an increased risk of postoperative hyperkalemia. Preoperative treatment with MR antagonists neither reduced nor increased the incidence of postoperative hyperkalemia in our study. Instead, renal protection strategies, such as volume expansion and avoidance of renal toxic drugs, are recommended to prevent postoperative hyperkalemia in high-risk patients with APA.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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References
12 Chiang WF, Cheng CJ, Wu ST, Sun GH, Lin MY, Sung CC & Lin SH. Incidence and factors of post-adrenalectomy hyperkalemia in patients...


