Clinical Implications of Renal Cyst in Primary Aldosteronism

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Abstract. The present study surveyed 69 patients with aldosteronoma to study the clinical implications of renal cysts demonstrated in computed tomography. Patients who had cysts (n=16, 23.2%) were older and had a longer duration of hypertension and more severe hypokalemia than those without cysts (n=53). Patients with cysts therefore had longer-term, more severe hypokalemia than those without cysts. Endogeneous creatinine clearance (Ccr), measured in 61 patients, was significantly lower in patients with cysts (58.4 ± 7.1 ml/min, n=16) than in those without cysts (77.3 ± 7.1 ml/min, n=45, P=0.0039). This significant difference was observed even after adjusting for covariables (age, duration of hypertension, and serum potassium) between the two groups by analysis of covariance (ANCOVA). No significant difference was observed in gender, blood pressure, serum creatinine, plasma aldosterone, or PRA. Age, serum potassium levels, and systolic and diastolic blood pressure were the significant determinants in predicting Ccr in a backward stepwise multiple regression analysis (r=0.505, n=61, P=0.0025). Cysts were graded into four classes on the basis of number and size. Cyst grading correlated negatively with Ccr at a Spearman rank correlation (r= -0.33, n=61, P=0.0103). The incidence of chronic renal failure was significantly higher in patients with cysts (18.8%) than in patients without (0%) in a Fischer's exact probability test (P=0.0107). Thus, both renal cysts and dysfunction arose and/or developed from common roots, i.e., the duration and severity of hypokalemia, in primary aldosteronism. In addition, we surveyed 27 patients with pheochromocytoma. Patients with renal cysts (n=8) had a significantly longer duration of hypertension than those without cysts. No significant difference was observed in Ccr between patients with and those without cysts. Thus, a significant link between renal cysts and Ccr was a specific feature of primary aldosteronism, but not of pheochromocytoma. In summary, the renal cysts in primary aldosteronism should be recognized as a significant complication representing the extent of renal injury and dysfunction.

Key words: Hypertension, Hypokalemia, Creatinine clearance, CT, Nephrocalcinosis

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PRIMARY aldosteronism causes hypertension, hypokalemia, and metabolic alkalosis. Each of these independent factors can potentially cause renal tissue injury. Hypertension causes nephrosclerosis (renal vascular and glomerular injuries) [1, 2]. Hypokalemia causes vacuolation, degeneration and hyperplasia of the tubular epithelium in medulla, and tubular dilatation and atrophy [1, 3]. Metabolic alkalosis has been reported to cause gross degeneration, lipoid changes, and calcification of the renal tubules [4]. The kidney is thus a sensitive organ that is injured in primary aldosteronism [1]. Torres et al. reported that abdominal computed tomography (CT) scans demonstrated a frequent association of renal cysts (44%) in 55 patients with primary aldosteronism (62% particularly in 26 patients with aldosteronoma) [5]. Lower plasma potassium levels and higher plasma aldosterone
levels were correlated with the extent of cystic disease. The size and number of cysts decreased markedly in some patients after the removal of an aldosteronoma. Renal cysts, especially in the renal medulla, have been thus considered a complication in primary aldosteronism, but subsequent reports have not confirmed this association [6,7].

The objectives of our present study are, by means of CT scans, to examine the frequency of renal cysts in Japanese patients with primary aldosteronism due to aldosteronoma, and to evaluate the factors contributing to the formation of cysts, together with the related clinical implications. We also studied whether renal calcification, another abnormal finding demonstrable in CT scans, is associated with primary aldosteronism.

Patients and Methods

Patients with primary aldosteronism or pheochromocytoma

Sixty-nine patients with aldosteronoma were surveyed, with a diagnosis of primary aldosteronism based on the observation of hypertension, hypokalemia, low plasma renin activity (PRA), high plasma aldosterone concentration (PAC), and normal urinary 17-OHCS and -KS excretions. In patients with PAC or PRA within the normal ranges, we conducted adrenal venin sampling, and a high aldosterone secretion was confirmed from the adenoma-bearing adrenal gland. Patients who had a history or abnormal laboratory findings suggesting renal disease before or during the onset of primary aldosteronism were excluded from this study. Sixty-two patients were eventually treated surgically and confirmed pathologically to have aldosteronoma. Seven were treated with medication. Twenty-seven patients with pheochromocytoma were also surveyed. The diagnosis of pheochromocytoma based on the observation of hypertension, high urinary catecholamines or their metabolites concentrations, and serum catecholamine concentrations. All patients were eventually treated surgically and confirmed pathologically to have pheochromocytoma. Data were obtained during their treatment at our hospital. Sodium chloride intake was restricted to 7 g/day. Almost all patients had a history of antihypertensive drug administration prior to being referred to our hospital on suspicion of having primary aldosteronism or pheochromocytoma. Medication was, in principle, stopped for at least two weeks in this study. In some patients we hesitated to completely stop treatment with antihypertensive drugs for too long a period. In such cases we worked to normalize blood pressure with drugs which had less influence on the hormonal status, e.g., calcium channel blockers [8], hydralazine, alpha blockers and methyldopa, and stopped these drugs at least overnight prior to and during the measurement of blood pressure, serum creatinine, 24-h endogeneous Ccr, and hormones. Blood pressure was recorded in the morning. PRA and PAC were measured by specific RIA as described previously [8]. The lowest detectable level of PRA was 0.03 ng/L·s. Suppressed PRA less than 0.03 was counted as 0.03 for statistical analysis. The normal range of PRA is between 0.14 and 0.83 ng/L·s, and that of PAC is between 61 and 416 pmol/L. In this analysis, we used the lowest serum potassium levels during periods in which patients were not treated with medication or were treated with antihypertensive drugs other than diuretics.

Computed tomography

Computed tomography (CT) conducted with a Toshiba TCT-60A or TCT900S, with sections taken 10 mm apart and a scanning time of 4.5 or 2 sec, detected aldosteronoma or pheochromocytoma with and without the intravenous administration of contrast material in all 69 patients. CT examination also enabled us to scan at least the upper two thirds of the entire kidney in which we could observe renal cysts. The incidence of cysts and calcification must therefore be evaluated as being lower than the actual incidence. Renal cysts were graded from zero to three by counting their number and size as follows: 0: absence of cysts; adding +1: presence of cyst; adding +1: multiple cysts; adding +1: presence of cyst with a diameter exceeding 2 cm. CT scans were repeated three years or more after surgical therapy (adrenalectomy) in some patients. Blood pressure was reevaluated at least three months or more after adrenalectomy in 12 patients with cysts and in 44 patients without cysts.

Statistical analysis

Data were shown as the mean ± SEM. The computer programs Stat View 4.0 and Super ANOVA
(Abacus Concepts, Inc, Berkeley, CA) were used for statistical analyses. An unpaired t-test or Mann Whitney U-test was used to determine the significance of differences between the two groups. An analysis of covariance (ANCOVA) was done when the dependent variable was suspected to have been affected by the covariable as well as the factor. Fisher's exact probability test was used to compare differences in gender distribution and in the frequency of renal cysts, calcification, chronic renal failure, and patients undergoing antihypertensive drug administration after adrenalectomy. Backward stepwise multiple regression was used to determine the influence of several independent variables, including age, blood pressure, duration of hypertension, PRA, PAC, and serum potassium, on Ccr and calcification. Pearson's method of regression analysis was used to study the correlation between age and duration of hypertension. A Spearman rank correlation was used to study the correlation between Ccr and the cyst grade. The statistical level of significance was P<0.05 for all tests used.

Results

Renal cysts in primary aldosteronism

Renal cysts were observed in 16 of the 69 patients (23.2%) with primary aldosteronism. Most of the patients with cysts (11/16) had multiple occurrences. Most of the cysts were observed at a point between the cortex and medulla, which made it difficult to determine whether the origin of a cyst was the cortex or the medulla (Fig. 1). Patients were divided to two groups based on cyst presence or absence. The two groups were then compared regarding gender, age, the duration of hypertension, blood pressure, serum potassium concentration, serum creatinine concentration, Ccr, PRA and PAC (Table 1). Patients with renal cysts were significantly older and had a longer duration of hypertension. Age (years) and the duration of hypertension (years) correlated significantly in Pearson's method of regression analysis: 

\[
\text{Duration} = -8.142 + 0.355 \times \text{(Age)} \quad (r=0.542, \, n=69, \, P<0.0001).
\]

Because the duration of hypertension may reflect the duration of the disease (primary aldosteronism), the age minus the duration of hypertension may indicate the age at disease onset. This estimated age of disease onset was almost identical for patients with and without cysts (Table 1). Patients with a longer history of the disease therefore tended to have renal cysts. Furthermore, patients with renal cysts had more severe hypokalemia and lower Ccr than those without renal cysts. A significant difference in Ccr between patients with and without cysts was still observed after adjustments for age, the duration of hypertension and serum potassium levels by using ANCOVA (Table 2).

Correlation between cysts and Ccr in primary aldosteronism

Among 61 patients whose Ccr was measured, nine (14.8%), i.e., five with renal cysts and four without renal cysts, had reduced Ccr (less than 50 ml/min). Three patients with renal cysts in particular also had chronic renal failure (Ccr of less than 30 ml/min), while none was evidenced in those without renal cysts. Because the serum creatinine concentration was normal in eight patients whose Ccr was not measured, they were judged not to have chronic renal failure. Patients with renal cysts therefore tended to suffer more frequently from chronic renal failure, i.e., 3/16 (18.8%) vs. 0/53 (0%), \((P=0.0234, \, n=69, \, \text{Fisher's exact probability test})\). Backward stepwise multiple regression analysis showed that aging (year), blood pressure (BP, mmHg), and serum potassium (mmol/L) were the significant determinants of Ccr (ml/min): 

\[
\text{Ccr} = 63.0 - 0.52 \times \text{(age)} + 11.8 \times \text{(serum potassium)} - 0.25 \times \text{(systolic BP)} + 0.44 \times \text{(diastolic BP)}, \quad r = 0.505, \, n = 61, \, P = 0.0025.
\]

Blood pressure contributed in complex ways, i.e., negatively by systolic BP and...
positively by diastolic BP. The duration of hypertension (F-value entered: 0.057), PRA (F-value entered: 0.122) and PAC (F-value entered: 1.781) was finally eliminated because none reached statistical significance (F-value entered: 4.0). To further clarify the relationship between Ccr and cysts, cysts were graded by the number and size observed in CT scans. A weak but significant correlation was found between Ccr and the cyst grade by a Spearman rank correlation ($\rho$ connected forties = −0.33, Tied $P$-value = 0.0103). All of three patients with chronic renal failure had multiple cysts.

**Postadrenalectomy changes in primary aldosteronism**

As mentioned earlier, there was no significant difference in blood pressure between patients with and without cysts. Blood pressure was measured three months or later after successful adrenalecto-

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**Table 1.** Clinical and laboratory findings in patients with primary aldosteronism, based on the presence or absence of renal cysts and calcification

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cyst Present</th>
<th>Cyst Absent</th>
<th>P value</th>
<th>Calculated Present</th>
<th>Calculated Absent</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>16</td>
<td>53</td>
<td>NS</td>
<td>13</td>
<td>56</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>8/8</td>
<td>20/33</td>
<td>NS</td>
<td>8/5</td>
<td>20/36</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>51.9 ± 3.1</td>
<td>45.0 ± 1.4</td>
<td>0.023</td>
<td>46.6 ± 3.9</td>
<td>46.7 ± 1.4</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of hypertension (yr)</td>
<td>11.7 ± 2.1</td>
<td>7.7 ± 0.9</td>
<td>0.0366</td>
<td>11.2 ± 2.1</td>
<td>7.7 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>185.6 ± 5.4</td>
<td>178.5 ± 4.2</td>
<td>NS</td>
<td>180.0 ± 7.3</td>
<td>180.0 ± 4.0</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>106.0 ± 3.7</td>
<td>105.1 ± 2.5</td>
<td>NS</td>
<td>101.9 ± 3.8</td>
<td>105.6 ± 2.4</td>
<td>NS</td>
</tr>
<tr>
<td>Lowest recorded serum potassium (mmol/L)</td>
<td>2.46 ± 0.16</td>
<td>2.78 ± 0.52</td>
<td>0.0449</td>
<td>2.65 ± 0.16</td>
<td>2.73 ± 0.08</td>
<td>NS</td>
</tr>
<tr>
<td>Plasma aldosterone (pmol/L)</td>
<td>1166 ± 246</td>
<td>986 ± 95</td>
<td>NS</td>
<td>1542 ± 272</td>
<td>940 ± 89</td>
<td>0.0087</td>
</tr>
<tr>
<td>Plasma renin activity (ng/L-s)</td>
<td>0.06 ± 0.02</td>
<td>0.06 ± 0.01</td>
<td>NS</td>
<td>0.08 ± 0.02</td>
<td>0.05 ± 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>123 ± 22</td>
<td>85 ± 3</td>
<td>NS</td>
<td>106 ± 9</td>
<td>88 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>Ccr (ml/min)#</td>
<td>58.4 ± 7.1</td>
<td>77.3 ± 2.7</td>
<td>0.0039</td>
<td>70.4 ± 7.9</td>
<td>73.4 ± 3.1</td>
<td>NS</td>
</tr>
<tr>
<td>Age at disease onset (yr)</td>
<td>40.3 ± 2.7</td>
<td>37.6 ± 1.2</td>
<td>NS</td>
<td>39.7 ± 3.0</td>
<td>37.7 ± 1.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant. Numbers in parentheses represent the range of variable. # Ccr was measured in fifteen patients with renal cysts and forty-six patients without cysts.

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**Table 2.** Comparison of Ccr, adjusted by covariable, in patients with and without cysts (ANCOVA)

<table>
<thead>
<tr>
<th>Covariable</th>
<th>Ccr adjusted by covariable (ml/min)</th>
<th>Patients with cyst</th>
<th>Patients without cyst</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>61.2 ± 5.5</td>
<td>76.4 ± 3.1</td>
<td>0.0201</td>
<td></td>
</tr>
<tr>
<td>Duration of hypertension (yr)</td>
<td>60.8 ± 5.5</td>
<td>76.5 ± 3.1</td>
<td>0.0175</td>
<td></td>
</tr>
<tr>
<td>Lowest recorded serum potassium (mmol/L)</td>
<td>59.7 ± 5.5</td>
<td>76.8 ± 3.1</td>
<td>0.009</td>
<td></td>
</tr>
</tbody>
</table>

Least squares means ± SEM are shown.
my in 12 patients with cysts and 44 patients without cysts (Table 3). Among these, six patients with cysts (50.0%) and 17 patients without cysts (38.6%) still needed antihypertensive drug administration. The proportion of patients on medication was not statistically different between the two groups.

There was also no significant difference in serum potassium or creatinine or blood pressure between the two groups after adrenalectomy (Table 3). When patients were examined at pre- and post-adrenalectomy by a paired t-test, serum creatinine in 11 patients with cysts did not change significantly, being from 133 ± 31 to 175 ± 75 μmol/L, but those in 29 patients without cysts increased slightly, from 84 ± 4 to 92 ± 6 μmol/L, \( P = 0.0436 \).

Seven patients with renal cysts were reexamined by CT scan three years or more after adrenalectomy. Cysts increased in either size or number in three patients, but did not change in four other patients. Three patients without cysts who were reexamined at least five years after adrenalectomy were all found to still be free of cysts.

### Renal cysts in pheochromocytoma

The incidence of renal cysts in patients with pheochromocytoma was 29.6% (8 in 27 patients). Patients with renal cysts had a significantly longer duration of hypertension than those without cysts (Table 4). Longer duration of hypertension and

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**Table 3.** Findings in patients after adrenalectomy based on the presence or absence of renal cysts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Present</th>
<th>Absent</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum potassium (mmol/L)</td>
<td>4.20 ± 0.13 (n=11)</td>
<td>4.33 ± 0.09 (n=29)</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>175 ± 75 (n=11)</td>
<td>92 ± 6 (n=29)</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>131.3 ± 4.1 (n=12)</td>
<td>130.7 ± 2.0 (n=44)</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic Bp (mmHg)</td>
<td>84.2 ± 2.7 (n=12)</td>
<td>83.9 ± 1.6 (n=44)</td>
<td>NS</td>
</tr>
</tbody>
</table>

These variables were examined three months or more after adrenalectomy.

**Table 4.** Clinical and laboratory findings in patients with pheochromocytoma based on the presence or absence of renal cysts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Present</th>
<th>Absent</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>8</td>
<td>19</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>4/4</td>
<td>9/10</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>58.6 ± 5.6 (36-77)</td>
<td>48.9 ± 3.2 (25-73)</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of hypertension (yr)</td>
<td>18.6 ± 5.2 (2-40)</td>
<td>3.7 ± 1.4 (1-21)</td>
<td>0.0041</td>
</tr>
<tr>
<td>Lowest recorded serum potassium (μmol/L)</td>
<td>4.03 ± 0.19 (3.2-4.9)</td>
<td>4.05-0.01 (3.3-4.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>83.10 ± 7.96 (53.04-132.6)</td>
<td>88.4 ± 4.42 (53.04-132.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Ccr (ml/min)</td>
<td>61.2 ± 4.6 (51.0-83.1)</td>
<td>72.2 ± 6.0 (36.5-100.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>153.1 ± 10.0 (112-180)</td>
<td>158.4 ± 8.4 (118-200)</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>91.7 ± 8.8 (60-120)</td>
<td>98.9 ± 5.1 (74-140)</td>
<td>NS</td>
</tr>
<tr>
<td>Age at disease onset (yr)</td>
<td>40.0 ± 6.7</td>
<td>43.4 ± 3.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant. Number in parentheses represent the range of variables. # Ccr was measured in seven patients with renal cysts and eleven patients without cysts.
also higher age may account for the relatively high incidence of renal cysts. There was no significant difference in other parameters shown in Table 4 including the serum creatinine concentration and Ccr. There was no patient with chronic renal failure.

Renal calcification in primary aldosteronism

Renal calcification was observed in 13 patients (18.8%) who had significantly higher PAC than patients without renal calcification (Table 1). Renal calcification was found mainly in the medullary region and was diffuse (n = 1) or solitary (n = 12). There was no difference between the two groups in any other parameters.

Discussion

Renal cysts were found in 23.2% of the patients we examined. The actual incidence should be higher than that when the entire kidney is scanned, but appeared still lower than the 62% reported by Torres et al. [5]. When we compared their patient profiles with ours, the only difference found was in the age of patients and in race. The average age in Torres' survey was 56.0 ± 11.2 (SD) years in patients without cysts and 58.9 ± 11.2 years in patients with cysts; this was 11 years older than our patients without cysts and 7 years older than ours with cysts. Because aging, especially after the age of 40, was a causative factor in the formation of renal cysts [9-11], the higher incidence of renal cysts in their study could be attributed partially to their older patient population. The incidence of simple renal cyst in the Japanese patient population, estimated by CT scan, was reported to be 14.4% between 40 and 49 years of age, 21.0% between 50 and 59 years of age, and 24.8% between 60 and 69 years of age [10]. Our present study thus failed to confirm that patients with primary aldosteronism had a higher frequency of renal cysts than simple cyst. This observation was compatible with that by others [6, 7]. The association with renal cysts, however, appeared to be one of the symptoms due to primary aldosteronism judging from the following evidence:

Patients with renal cysts were found to be older, to have a longer duration of hypertension, to have more severe hypokalemia, and to show reduced renal function when compared to those without cysts. Judging from age and the duration of hypertension, the age at disease onset appeared almost the same in the two groups. Long-term, severe hypokalemia thus contributed to the formation of renal cysts as a specific factor in primary aldosteronism. A low potassium concentration in a medium stimulates the proliferation of African green monkey kidney cells in a culture [12]. Hypokalemia as a mitogen thus causes hyperplasia of the collecting tubular cells in the outer medulla, resulting in the obstruction of the tubular lumen and the formation of cysts [3, 13]. Renal cysts in primary aldosteronism were therefore expected to develop in the medulla [5], but their origin was found to be difficult to identify in CT scans because they were seen across both the cortex and medulla in this study (Fig. 1).

Torres et al. reported identical serum creatinine levels in patients with and without cysts [5]. On the other hand, we observed a tendency for patients with cysts to have higher serum creatinine levels, although not significantly so. We further examined glomerular filtration rates in most patients (n=61) and observed lower Ccr levels in patients with cysts. Aging, the duration of hypertension, and hypokalemia were thus not only causative factors in renal cysts but also factors linked to renal function. Aging itself can reduce Ccr [14, 15]. Its effect was, however, weak in the Japanese study, i.e., 109.7 ± 5.1 (males) and 92.0 ± 4.1 ml/min (females) between 41 and 50 years of age and 97.6 ± 5.5 (males) and 83.5 ± 4.6 ml/min (females) between 51 and 60 years of age [14]. Patients with primary aldosteronism in this study had lower Ccr than the average Japanese. Of these, patients with cysts had lower Ccr levels than those without cysts. Several statistical analyses suggested that the difference in Ccr between patients with and without cysts appeared attributable to the difference in the duration and severity of hypokalemia, in addition to the difference in the simple nonspecific factor of aging. Ccr was, at first, actually lower in patients with cysts than in patients without cysts even after eliminating factors of age and the duration of hypertension or hypokalemia in ANCOVA. Second, the rough grading of cysts correlated weakly but significantly with Ccr. Third, all of the patients with chronic renal failure had multiple cysts, i.e., the incidence of chronic renal failure was significantly higher in patients with cysts (18.8%) than in those without (0%). Fourth, a significant linkage between Ccr and cyst was found in primary aldosteronism, but
not in pheochromocytoma. All of these observations suggest that renal cysts are an indication of the possible extent of renal injury which could eventually lead to renal failure. Furthermore, a stepwise multiple regression analysis suggested that, in addition to age and hypokalemia, systolic and diastolic blood pressure also affected Ccr. Hypertension causes nephrosclerosis and reduces the glomerular filtration rate after a significant duration [1, 2]. We therefore expected that systolic blood pressure would affect Ccr negatively, but unexpectedly found that diastolic blood pressure had a positive effect. From our present observations, we could not clarify why diastolic blood pressure affected Ccr positively. Because the correlation coefficient (r) was comparatively low (0.505), other unknown factors may have affected Ccr. The contribution of diastolic blood pressure should be reevaluated if such unknown factor or factors are identified in future. The involvement of the complex influence of blood pressure and other unknown factors thus remains to be clarified.

We observed three patients with Ccr less than 30 ml/min (4.3%). There was no evidence to doubt the fact that chronic renal failure was an outcome of primary aldosteronism in these patients. All of them received surgical treatment, and their serum creatinine decreased in two patients but increased in one patient who later needed hemodialysis. This incidence of chronic renal failure appeared high compared to that in a recent retrospective analysis of 82 patients with primary aldosteronism which reported six patients (7.3%) with a history of cardiovascular events, five (6.1%) with cerebrovascular events and none with chronic renal failure [7]. But Beever's et al. reported that 31 (22.8%) of 136 patients had vascular complications and 4 (2.9%) had evidence of malignant-phase hypertension [16]. Young et al. also reported 12 patients with vascular complications and 6 patients with chronic renal failure [2]. These observations suggest that some primary aldosteronism patients may have vascular complications and chronic renal failure if they are not treated appropriately. Renal cysts were also frequently observed in patients with end-stage renal disease, especially in patients on dialysis [17]. Such acquired cysts were caused by epithelial hyperplasia of the tubules [18]. A difference between end-stage renal disease and primary aldosteronism should be noted, in that the corresponding cells were different, i.e., the proximal tubules in end-stage renal disease and the collecting tubules in primary aldosteronism. The results of the present study also suggested the possibility that renal dysfunction may be prevented by treating hypokalemia at an early stage of the disease. Although Torres et al. reported a decrease in the grade of cysts after adrenalectomy in some patients [5], we found no significant effect of adrenalectomy on cysts in our preliminary study. We observed slight but significant increases in serum creatinine after adrenalectomy in patients without cysts, but not in patients with cysts. Although this preliminary observation is difficult to interpret, it suggests that adrenalectomy may help preserve renal function even in patients with reduced renal function. Further studies with larger patient populations are thus needed to clarify whether the treatment of hypokalemia can reduce the grade of cysts and improve renal function (Ccr). Although excision of cyst or needle aspiration of cystic fluid may improve hypertension [9, 19, 20], such treatments were not applied in our cases because of the small size of the cysts.

Patients with renal calcification had higher PAC than those without. The syndrome of apparent mineralocorticoid excess [21] and Liddle's syndrome [22] were also reported to have nephrosclerosis. Both syndromes have pathophysiological conditions similar to that of primary aldosteronism, i.e., hypertension, hypokalemia, suppressed PRA and metabolic alkalosis, but PAC was normal or suppressed. Taken together, the results suggested that hyperaldosteronism-induced change, especially metabolic alkalosis, may be related to nephrocalcinosis. Metabolic alkalosis was a potential factor in causing renal calcification in patients with pyloric stenosis [4]. Pyelonephritis also potentially causes renal calcification [23] and was reportedly found in a significant number of patients with primary aldosteronism [23, 24]. Because patients with calcification in our study had no history of pyelonephritis, it seemed unlikely that calcification was an outcome of it. Although metabolic alkalosis due to profound aldosteronism could be a candidate for causing renal calcification, no direct evidence of this is available. Of interest was the fact that cysts and calcification were related to different independent variables, indicating that both changes had different causes and meanings. Our study suggested that nephrocalcinosis did not reflect renal injury.

In summary, renal cysts in primary aldosteronism were significant indicators of the extent of renal in-
jury and dysfunction, especially in the medulla. The duration and severity of hypokalemia were the major factors in the cause and development of renal cysts and dysfunction. CT scans and other imaging techniques can also serve as another tool in evaluating the pathological status of kidneys, especially in the outer medulla, in primary aldosteronism.

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References