Cardiovascular Complications Associated With Primary Aldosteronism
A Controlled Cross-Sectional Study

Sébastien Savard, Laurence Amar, Pierre-François Plouin, Olivier Steichen

Abstract—A higher risk of cardiovascular events has been reported in patients with primary aldosteronism (PA) than in otherwise similar patients with essential hypertension (EH). However, the evidence is limited by small sample size and potential confounding factors. We, therefore, compared the prevalence of cardiovascular events in 459 patients with PA diagnosed in our hypertension unit from 2001 to 2006 and 1290 controls with EH. PA cases and EH controls were individually matched for sex, age (±2 years), and office systolic blood pressure (±10 mm Hg). Patients with PA and EH differed significantly in duration of hypertension, serum potassium, plasma aldosterone and plasma renin concentrations, aldosterone-to-renin ratio, and urinary aldosterone concentration (P<0.001 for all comparisons). The prevalence of electrocardiographic and echocardiographic left ventricular hypertrophy was about twice higher in patients with PA even after adjustment for hypertension duration. PA patients also had a significantly higher prevalence of coronary artery disease (adjusted odds ratio, 1.9), nonfatal myocardial infarction (adjusted odds ratio, 2.6), heart failure (adjusted odds ratio, 2.9), and atrial fibrillation (adjusted odds ratio, 5.0). The risks associated with PA were similar across levels of serum potassium and plasma aldosterone. To conclude, patients with PA are more likely to have had a cardiovascular complication at diagnosis than otherwise similar patients with EH. Target organ damage and complications disproportionate to blood pressure should be considered as an additional argument for suspecting PA in a given individual and possibly for broadening the scope of screening at the population level. (Hypertension. 2013;62:00-00.) Online Data Supplement

Key Words: atrial fibrillation coronary artery disease heart failure hyperaldosteronism hypertension hyptertrophy, left ventricular myocardial infarction

Primary aldosteronism (PA) is the most frequent endocrine cause of secondary hypertension, affecting ≈10% of patients referred to specialized clinics. It is characterized by autonomous aldosterone secretion, resulting in hypokalemia, sodium reabsorption, and fluid retention. In addition to these well-known effects, there is compelling evidence to suggest that prolonged exposure to high aldosterone concentrations has a deleterious effect on cardiovascular tissues and is associated with target organ damage, independently of blood pressure (BP). Previous studies have been limited by small sample sizes and potential confounders not accounted for in the study design or analysis.

The aim of this study was to compare the prevalence of cardiovascular events in a large group of current patients with PA and suitably matched controls with essential hypertension (EH) to confirm the adverse cardiovascular effects of PA.

Patients and Methods

Data Retrieval and Patient Selection
Patient selection and data retrieval have been described elsewhere. Briefly, all patients referred to our hypertension referral center and newly diagnosed with PA between January 1, 2001, and December 31, 2006, were included. Patients with excess mineralocorticoid were identified from an electronic health record database established in 1975 and based on standardized questionnaires completed prospectively by the physician for each patient referred to our unit. Four other databases from the biochemistry, genetics, hypertension, and radiology departments were also queried to ensure the retrieval of all cases referred during this time period. The retrieved cases were reviewed and included in the final analysis if they fulfilled the diagnostic criteria for PA described below.

Controls were adult patients with EH referred to our unit during the same time period and identified with the same electronic health record database. EH controls were considered suitable for analysis if they were not pregnant and if diagnostic analysis at the hospital was complete, included a normal aldosterone-to-renin ratio (ARR), and revealed no secondary cause of hypertension.

Received January 18, 2013; first decision February 2, 2013; revision accepted May 20, 2013.
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The online-only Data Supplement is available with this article at http://hyper.ahajournals.org/lookup/suppl/doi:10.1161/HYPERTENSIONAHA.113.01060/-/DC1.
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Hypertension is available at http://hyper.ahajournals.org DOI: 10.1161/HYPERTENSIONAHA.113.01060
Baseline clinical, biochemical, and imaging data obtained at the first diagnostic analysis within the hospital were extracted from the hospital database and used for analysis. Missing data were collected manually from medical charts by 2 investigators (S.S. and O.S.).

Biochemical Methods
Hormonal assessment was conducted as previously reported.²⁻⁴ Renin and aldosterone determinations were performed after the withdrawal of antihypertensive drugs that might interfere with the results and with oral potassium supplementation if plasma potassium was <3.5 mmol/L. Plasma and urinary aldosterone concentrations were determined by radioimmunoassay (Coat-A-Count; Siemens Medical Solutions Diagnostics, Saint-Denis, France); the 24-hour urinary excretion of aldosterone was determined as the sum of free aldosterone and aldosterone from the hydrolysis of aldosterone-18-glucuronide at pH 1.0. Plasma active renin concentration was determined by chemiluminescence immunoassay (LIAISON; Diasorin, Antony, France). Plasma and urinary potassium concentrations were determined by indirect potentiometry (Unicel DxC 800 system; Beckman Coulter, Villepinte, France). In patients with a family history of hypertension, genetic tests were performed to exclude glucocorticoid-remediable aldosteronism. All other biochemical variables were assayed in plasma or serum by standard methods. Estimated glomerular filtration rate was calculated with the modification of diet in renal disease formula.¹⁰

Diagnostic Criteria and Patient Classification

Diagnosis of PA
PA was diagnosed if the ARR obtained in standardized conditions was >64 pmol/mL (3.6 ng/ng) on 2 occasions and if plasma aldosterone concentration was >550 pmol/L (20 ng/dL) in the standing or sitting position or >500 pmol/L (18 ng/dL) in the supine position or urinary aldosterone excretion was >63 nmol/d (23 μg/d). For ARR calculation, active renin concentrations <5 mIU/L (3 ng/L) were set to 5 mIU/L to prevent ARR overestimation when active renin was undetectable or present at very low concentrations. The distribution of patients according to adrenal venous sampling and computed tomography results has been reported elsewhere and subsequently updated.¹³ The outcome of surgery in operated patients has also been reported elsewhere.¹¹

BP measurements
Three BP measurements were obtained in the sitting position, with a validated semiautomatic manometer (Omron 705CP), leaving a 5-minute rest period between measurements. Office BP was determined by calculating the mean of the second and third measurements, as described previously.¹²

Definition of Left Ventricular Hypertrophy
Twelve-lead ECG recordings were taken with 25 mm/s and 0.1 mV/mm standardization, as part of the initial evaluation, and were used to determine the prevalence of left ventricular hypertrophy (LVH) on the basis of electric criteria. The cutoff point was 35 mm for the Sokolow–Lyon index (RV₅ or RV₆+SV₁)¹³,¹⁴ and 28 mm in men and 20 mm in women for the sex-specific Cornell voltage index (RaVL+SV₃), values greater than these thresholds indicating the presence of LVH.¹⁵ Two-dimensional echocardiography was performed in most patients as part of the initial evaluation. Left ventricular mass (LVM) was determined from M-mode recordings and indexed either to body surface area (g/m²) or height to the power of 2.7 (g/m³).¹⁶ Echographic LVH was defined as an LVM index >115 g/m² in men or >95 g/m² in women¹⁷ after normalization with respect to body surface area and as an LVM index >50 g/m² in men or >47 g/m² in women¹⁷ after normalization with respect to height.¹² LVH was described as concentric if relative wall thickness was >0.42, and eccentric otherwise.

Definition of Cardiovascular Events
The patients’ history of cardiovascular events (as reported by the patient or the referring physician) at the time of the first visit to our center (before PA diagnosis) was collected and stored in the database. All reported cardiovascular events—atrial fibrillation (AF), nonfatal myocardial infarction (MI), coronary artery disease, or heart failure—in cases or controls were validated through medical chart review by a single investigator (S.S.).

Atrial Fibrillation
AF diagnosis was based on current or previously documented typical supraventricular arrhythmia on ECG, characterized by the replacement of consistent P waves by rapid oscillations or fibrillatory waves associated with an irregular ventricular response.¹⁸

Myocardial Infarction
Prior nonfatal MI was defined as a positive medical history and presence of pathological Q waves (≥0.03 seconds and ≥1 mm deep) for contiguous ECG leads and imaging evidence (echocardiography, MRI, or myocardial perfusion scintigraphy) of a regional loss of viable myocardium as a result of myocardial thinning and a failure to contract.¹⁹

Coronary Artery Disease
Coronary artery disease was considered to be present in patients with a positive medical history of angina or MI (previously defined) with objectively recorded ischemia on myocardial perfusion scintigraphy or >50% coronary stenosis on coronary angiography, with or without prior treatment by percutaneous angioplasty or bypass surgery.

Heart Failure
Heart failure diagnosis was validated in patients with a history of pulmonary congestion, decompensated heart failure, or exertional dyspnea associated with a left ventricular ejection fraction on echocardiography <55% by the 2-dimensional method.¹⁶ A decreased left ventricular ejection fraction in the absence of a clinical history of heart failure was not considered sufficient to affirm this diagnosis.

Statistical Methods
Each case was paired with ≤3 controls, individually matched for sex, age (±2 years), and systolic BP (±10 mm Hg). Conditional logistic regression (Wald test; P<0.05 considered significant) was used for matched analyses. Conformity to a linear gradient was graphically checked for continuous variables, and polynomial or logarithmic transformations were performed when necessary. Odds ratios (ORs) were calculated by conditional logistic regression, and interactions with sex and plasma potassium (≤ or ≥2.5 mmol/L) and plasma aldosterone concentrations (< or ≥23.5 nmol/L) were systematically tested and considered significant if P<0.01. All statistical analyses were performed with Stata 9.2 (StataCorp, College Station, TX).

Results
Querying of the database identified 459 cases with PA and a control group of 1290 patients with EH.

Characteristics of the Patients at the First Visit
The baseline characteristics of the patients at their first hospital evaluation are shown in Table 1. As a result of the matching process, age, sex, and systolic BP were similar between cases and controls. The PA cases had a longer duration of hypertension than EH controls, a higher prevalence of estimated glomerular filtration rate <60 mL/min per 1.73 m², lower serum potassium and plasma active renin concentrations, higher plasma and urinary aldosterone concentrations, and a higher ARR than EH controls (P<0.001 for all comparisons).

Left Ventricular Hypertrophy
Patients with and without ECG data did not differ significantly in terms of age, sex, hypertension duration, BP, body mass index, or estimated glomerular filtration rate. Patients with and without echocardiography results did not differ significantly
for these variables, but those with echocardiography results were more likely to have high Sokolow–Lyon and Cornell indices than patients without echocardiography results. A comparison of electrocardiographic and echocardiographic LVH between patients with PA and matched controls is shown in Table S1 in the online-only Data Supplement. All indices revealed a higher prevalence of LVH in patients with PA than in matched EH controls. The OR was not significantly modified by adjustment for hypertension duration and did not differ between subgroups of PA patients defined on the basis of sex or serum potassium or plasma aldosterone concentrations (interaction tests not significant).

**Cardiovascular Events**

A history of AF, MI, coronary artery disease, or heart failure was more frequently found at first visit in patients with PA than in matched controls (Table 2). These ORs were not significantly modified by adjustment for hypertension duration as a continuous variable or dichotomized (≤10 years, >10 years), see Table 2) and did not differ between subgroups of PA patients defined on the basis of sex and serum potassium or plasma aldosterone concentrations (interaction tests not significant).

**Discussion**

This single-center study included a large number of contemporary, well-characterized PA patients and controls with EH properly matched for age, sex, and systolic BP. Despite secular trends toward improvements in the control of BP and other cardiovascular risk factors, this study showed, like previous investigations, that PA is associated with a higher prevalence of LVH and cardiovascular complications than EH, regardless of BP level and hypertension duration. Furthermore, no heterogeneity of effect was observed between subgroups of PA patients defined on the basis of serum potassium or plasma aldosterone concentrations.

**PA and LVH**

Structural and functional cardiac modifications in PA patients have recently been the subject of a systematic review. The sample size of retrieved studies was limited (only 4 studies with >50 patients). In 14 of 18 studies, LVM was greater in PA patients compared with EH controls matched for age, sex, and BP. Our study confirmed on a much larger sample size, allowing multivariable adjustments and more precise estimates that, regardless of the criteria used, LVH is about twice as frequent in patients with PA as in otherwise similar patients with EH.

**Table 1.** Baseline Characteristics of Patients With Primary Aldosteronism and Controls With Essential Hypertension

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Primary Aldosteronism</th>
<th>Essential Hypertension</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation, y</td>
<td>459 51±10.2</td>
<td>1290 51.3±10.3</td>
<td>…</td>
</tr>
<tr>
<td>Sex, male</td>
<td>459 306 (67%)</td>
<td>1290 841 (65%)</td>
<td>…</td>
</tr>
<tr>
<td>Systolic blood pressure at first visit, mm Hg</td>
<td>459 151±24.4</td>
<td>1290 149.9±22.0</td>
<td>…</td>
</tr>
<tr>
<td>Diastolic blood pressure at first visit, mm Hg</td>
<td>459 87.7±13.1</td>
<td>1290 87.1±12.6</td>
<td>0.78</td>
</tr>
<tr>
<td>Current treatment for hypertension</td>
<td>428 314 (73%)</td>
<td>1181 876 (74%)</td>
<td>0.59</td>
</tr>
<tr>
<td>No. of antihypertensive classes</td>
<td>428 1.7±1.5</td>
<td>1181 1.7±1.4</td>
<td>0.11</td>
</tr>
<tr>
<td>Duration of hypertension, y</td>
<td>437 10.9±9.1</td>
<td>1239 8.5±9.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>433 74 (17%)</td>
<td>1243 178 (14%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>458 28.2±4.8</td>
<td>1290 27.8±5.1</td>
<td>0.20</td>
</tr>
<tr>
<td>Ever smoker</td>
<td>317 141 (44%)</td>
<td>1255 642 (51%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Current smokers</td>
<td>339 51 (15%)</td>
<td>1241 178 (14%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Blood glucose, mmol/L</td>
<td>458 5.8±1.9</td>
<td>1276 5.8±1.5</td>
<td>0.67</td>
</tr>
<tr>
<td>Creatinine, µmol/L</td>
<td>459 88±35.4</td>
<td>1285 83.8±27.4</td>
<td>0.005</td>
</tr>
<tr>
<td>Creatinine clearance (MDRD), mL/min per 1.73 m²</td>
<td>459 85.1±24.1</td>
<td>1285 86.7±20.7</td>
<td>0.15</td>
</tr>
<tr>
<td>MDRD &lt;60 mL/min per 1.73 m²</td>
<td>459 58 (13%)</td>
<td>1285 94 (7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum potassium, mmol/L</td>
<td>459 3.4±0.5</td>
<td>1284 3.8±0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Plasma aldosterone, pmol/L</td>
<td>458 674.8±451.3</td>
<td>1280 279.1±170.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Plasma active renin, mU/L</td>
<td>458 3.8±2.4</td>
<td>1280 27.5±138.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aldosterone/renin ratio</td>
<td>458 122.3±84.5</td>
<td>1280 29.5±21.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urinary aldosterone, mmol/24 h</td>
<td>393 90±50.4</td>
<td>815 41.3±28.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum total cholesterol, mmol/L</td>
<td>457 5.0±1.0</td>
<td>1274 5.0±1.0</td>
<td>0.36</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>457 1.3±0.9</td>
<td>1273 1.3±0.9</td>
<td>0.73</td>
</tr>
</tbody>
</table>

The number of patients (No.) available for analysis is shown for each variable. The values shown are the numbers of patients (percentage) for binary variables and means±SD for quantitative variables. To convert the value for aldosterone to ng/dL, multiply by 0.0361. To convert the value for active renin concentration to ng/L, multiply by 0.6. MDRD indicates modification of diet in renal disease.
long been considered a benign form of hypertension associated with a low frequency of cardiovascular complications. However, cross-sectional studies have reported cardiovascular complications in 14% to 35% of patients with PA. These studies are summarized in Table 3.

Despite the higher frequency of cardiovascular complications in patients with PA than in those with EH, the absolute prevalence and the difference from matched controls were smaller than those previously reported. For instance, our results differ from those previously observed—1997 to 1999 versus 2001 to 2006—in the same clinical environment. Better control of hypertension and other cardiovascular risk factors in primary prevention or earlier referral to specialized hypertension clinics might explain this trend. These hypotheses are consistent with the 20 mm Hg lower mean BP (systolic hypertension clinics might explain this trend. These hypotheses are consistent with the 20 mm Hg lower mean BP (systolic and diastolic) observed in our study. They are also consistent with the secular trend observed in the general population over the past 10 years. It is also possible that the level of some effect modifiers have changed in recent years. For instance, it is likely that lower dietary salt intake decreases the deleterious effects of aldosterone. The residual excess risk may be attributable to a direct effect of hyperaldosteronism on target organs or to unmeasured hemodynamic confounders, such as higher nighttime BP, although it has been reported that nighttime BP in patients with PA is not consistently higher than that in EH patients with similar daytime BP.

Cardiovascular complications were not significantly more frequent in PA patients with low plasma potassium, suggesting that the higher frequency of cardiovascular complications in PA patients did not result from an indirect effect mediated by plasma potassium. Unlike previous studies, we found that cardiovascular complications were not more frequent in PA patients with higher aldosterone levels, suggesting that aldosterone levels in PA patients are over a threshold above which there is no further increase in cardiovascular complications. However, our subgroup analyses have limited power because of the small number of events.

Aldosterone and Target Organ Damage

In addition to its effect on BP and serum potassium concentration, aldosterone (or mineralocorticoid receptor activation) has proinflammatory, prothrombotic, and profibrotic effects, contributing to target organ damage, as outlined in recent reviews. The mechanisms by which aldosterone exerts its deleterious effect are outside the scope of this clinical study but include chronic intravascular fluid retention, oxidative stress, endothelial dysfunction, inflammation, remodeling, hypertrophy, and fibrosis. These mechanisms lead to structural abnormalities, including an increase in arterial wall stiffness and carotid intima-media thickness, the formation of carotid plaques, and myocardial fibrosis.

Many hypotheses have been proposed to explain the higher frequency of AF in PA patients: low potassium concentration per se, the increase in left atrial volume, the excess LVMI secondary to both excess aldosterone and hypertension, myocardial fibrosis or ischemia, magnesium losses, and catecholamine potentiation. Furthermore, the proarrhythmic properties of aldosterone may be mediated by an increase in sympathetic drive, a decrease in heart rate variability, a disturbance of baroreceptor function, blunted myocardial norepinephrine uptake, and changes in electrolyte homeostasis.

**Strengths and Weaknesses of the Study**

This study is based on a large number of consecutive patients diagnosed with PA by standardized diagnostic procedures after the year 2000, for whom evaluation was conducted at a single hypertension referral center. PA and EH patients were individually matched for 3 potent cardiovascular risk factors (age, sex, and BP), and analyses were adjusted for an additional unbalanced risk factor (hypertension duration), ensuring valid comparisons. However, some limitations of our study should be highlighted. First, our diagnostic criteria differ from those used in other centers, and this may impact the ORs observed in our study. However, the direction and magnitude of the effect are similar to those previously observed in other settings. Second, potential confounders may remain, despite this careful matching and further adjustments during analyses. Third, we did not look for an effect difference between unilateral and bilateral PA because our population could not be entirely subclassified. However, we did evaluate serum aldosterone and potassium as potential effect modifiers. Fourth, multiple comparisons increase the risk of P values being <0.05 because of chance alone. However, highly significant differences (P<0.001) may be considered reliable. Fifth, our study is retrospective with the limitations inherent to such studies, including missing data. Nevertheless, the computerized and structured data collection for clinical care resulted in there being <15% missing data for clinical variables, except for smoking status (30% missing data) and echocardiography (27% missing data) in patients with PA. Furthermore, the medical charts of all cases and controls for whom cardiovascular events were reported were systematically reviewed by one of the authors (S.S.).

**Table 2. Prevalence of Cardiovascular Events Reported at First Visit in Patients With Primary Hyperaldosteronism and Patients With Essential Hypertension**

<table>
<thead>
<tr>
<th>Cardiovascular Events</th>
<th>Primary Aldosteronism</th>
<th>Essential Hypertension</th>
<th>Unadjusted OR (95% CI)</th>
<th>Unadjusted P Value</th>
<th>Adjusted OR (95% CI)</th>
<th>Adjusted P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted OR</td>
<td>Adjusted OR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>459</td>
<td>18 (3.9)</td>
<td>1289</td>
<td>14 (1.1)</td>
<td>4.3 (2.0–9.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>459</td>
<td>20 (4.4)</td>
<td>1290</td>
<td>22 (1.7)</td>
<td>2.8 (1.4–5.4)</td>
<td>0.003</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>459</td>
<td>20 (5.7)</td>
<td>1290</td>
<td>36 (2.8)</td>
<td>2.2 (1.2–3.7)</td>
<td>0.006</td>
</tr>
<tr>
<td>Heart failure</td>
<td>459</td>
<td>19 (4.1)</td>
<td>1290</td>
<td>16 (1.2)</td>
<td>3.5 (1.7–6.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The number of patients (No.) available for analysis is shown for each variable. The values shown are the numbers of patients (percentage). Adjusted analysis accounts for hypertension duration as a continuous variable. CI indicates confidence interval; and OR, odds ratio.
Table 3. Published Series on Primary Aldosteronism and Cardiovascular Complications

<table>
<thead>
<tr>
<th>Published Series</th>
<th>Number of patients</th>
<th>Blood Pressure</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takeda et al²⁵</td>
<td>224 patients with surgically proven APA</td>
<td>170±26/94±15</td>
<td>Myocardial infarction (1.8% vs 4.0%) Heart failure (3.6% vs 4.0%)</td>
</tr>
<tr>
<td>Milliez et al⁴</td>
<td>124 patients with PA</td>
<td>176±23/107±14</td>
<td>Myocardial infarction (4.0% vs 0.6%; OR, 6.5) Atrial fibrillation (7.3% vs 0.6%; OR, 12.1)</td>
</tr>
<tr>
<td>Catena et al⁵⁷</td>
<td>54 patients with PA</td>
<td>167±16/103±9</td>
<td>Cardiovascular events more frequent in PA patients (35% vs 11%; OR, 4.61; P&lt;0.001) Sustained arrhythmias (15% vs 3%; OR, 4.93) Cerebrovascular events (11% vs 3%; OR, 4.36) Coronary heart disease (20% vs 8%; OR, 2.80)</td>
</tr>
<tr>
<td>Current study</td>
<td>459 patients with PA</td>
<td>151±24/88±13</td>
<td>Myocardial infarction (4.4% vs 1.7%; OR, 2.8) Atrial fibrillation (3.9% vs 1.1%; OR, 4.3) Coronary artery disease (5.7% vs 2.6%; OR, 2.2) Heart failure (4.1% vs 1.2%; OR, 3.5)</td>
</tr>
</tbody>
</table>

APA indicates aldosterone-producing adenoma; BMI, body mass index; BP, blood pressure; EH, essential hypertension; HTN, hypertension; IBI, idiopathic bilateral hyperplasia; OR, odds ratio; and PA, primary aldosteronism.

Perspectives

We show that patients with PA more frequently have LVH and are at higher risk of cardiovascular complications than matched EH controls. This finding is consistent with previous data suggesting that the higher risk of cardiovascular events associated with PA is at least partly independent of BP. Specific surgical and pharmacological treatments are available to decrease or counteract the excessively high aldosterone levels in this condition. It is, therefore, of prime importance to identify these patients early to prevent or reverse cardiovascular complications. Furthermore, target organ damage disproportionate to BP should be considered as an additional argument for suspecting PA in a given individual and possibly for broadening the scope of screening at the population level.

Sources of Funding

Sébastien Savard received financial support from la Société Québécoise d’Hypertension Artérielle, la Société Québécoise de Néphrologie, la Faculté de Médecine de l’Université Laval (McLaughlin Scholarship Program), and from La Fondation du Centre Hospitalier Universitaire de Québec for his postdoctoral fellowship.

Disclosures

None.

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Novelty and Significance

What Is New?

• This study provides current estimates of the cardiovascular risk excess in 459 patients with primary aldosteronism compared with 1290 matched patients with essential hypertension.

What Is Relevant?

• Previous small studies have shown increased cardiovascular risk in primary aldosteronism. However, patients are diagnosed with less severe primary aldosteronism on average since the widespread use of the aldosterone renin ratio, and this may decrease cardiovascular risk.

Summary

The odds ratios of complications in primary aldosteronism compared with essential hypertension were ≈2 for left ventricular hypertrophy and coronary artery disease, ≈3 for myocardial infarction and heart failure, and ≈5 for atrial fibrillation.
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*Hypertension.* published online June 10, 2013;

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/early/2013/06/10/HYPERTENSIONAHA.113.01060

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Cardiovascular complications associated with primary aldosteronism: a controlled cross-sectional study

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\textbf{Abbreviated title:} Primary aldosteronism and cardiovascular complications

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Online Table S1. Comparison of left ventricular hypertrophy between patients with primary aldosteronism and patients with essential hypertension

<table>
<thead>
<tr>
<th>Left ventricular hypertrophy</th>
<th>Primary aldosteronism</th>
<th>Essential hypertension</th>
<th>Unadjusted OR [95% CI]</th>
<th>Unadjusted p</th>
<th>Adjusted OR [95% CI]</th>
<th>Adjusted p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Electrical criteria</strong></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Sokolow index</td>
<td>383</td>
<td>1142</td>
<td>23.5 ± 8.5</td>
<td>--</td>
<td>0.001</td>
<td>--</td>
</tr>
<tr>
<td>Sokolow index &gt;35</td>
<td>389</td>
<td>1156</td>
<td>14 (9.9%)</td>
<td>1.8 [1.3 – 2.6]</td>
<td>0.001</td>
<td>1.9 [1.3 – 2.7]</td>
</tr>
<tr>
<td>Cornell index</td>
<td>264</td>
<td>828</td>
<td>20.1 ± 7.6</td>
<td>--</td>
<td>&lt;0.001</td>
<td>--</td>
</tr>
<tr>
<td>Cornell index &gt;20 (women) or &gt;28 (men)</td>
<td>264</td>
<td>828</td>
<td>98 (11.8%)</td>
<td>1.8 [1.2 – 2.8]</td>
<td>0.007</td>
<td>1.7 [1.1 – 2.6]</td>
</tr>
<tr>
<td><strong>Echographic criteria #1</strong></td>
<td></td>
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</tr>
<tr>
<td>Left ventricular mass index (g/m²)</td>
<td>334</td>
<td>949</td>
<td>94.7 ± 27.5</td>
<td>--</td>
<td>&lt; 0.001</td>
<td>--</td>
</tr>
<tr>
<td>Left ventricular hypertrophy³</td>
<td>335</td>
<td>949</td>
<td>232 (24.4%)</td>
<td>2.2 [1.7 – 2.9]</td>
<td>&lt; 0.001</td>
<td>2.3 [1.7 – 3.0]</td>
</tr>
<tr>
<td>Concentric⁵</td>
<td>334</td>
<td>951</td>
<td>125 (13.1%)</td>
<td>1.8 [1.3 – 2.6]</td>
<td>&lt; 0.001</td>
<td>1.7 [1.2 – 2.4]</td>
</tr>
<tr>
<td>Eccentric⁶</td>
<td>334</td>
<td>949</td>
<td>107 (11.3%)</td>
<td>2.0 [1.5 – 2.9]</td>
<td>&lt; 0.001</td>
<td>2.2 [1.6 – 3.2]</td>
</tr>
<tr>
<td><strong>Echographic criteria #2</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular mass index (g/m²)</td>
<td>334</td>
<td>949</td>
<td>43.8 ± 13.7</td>
<td>--</td>
<td>&lt; 0.001</td>
<td>--</td>
</tr>
<tr>
<td>Left ventricular hypertrophy⁷</td>
<td>335</td>
<td>949</td>
<td>268 (28.2%)</td>
<td>2.3 [1.8 – 3.0]</td>
<td>&lt; 0.001</td>
<td>2.2 [1.7 – 2.9]</td>
</tr>
<tr>
<td>Concentric⁸</td>
<td>334</td>
<td>951</td>
<td>142 (14.9%)</td>
<td>1.6 [1.2 – 2.2]</td>
<td>0.003</td>
<td>1.5 [1.1 – 2.1]</td>
</tr>
<tr>
<td>Eccentric⁹</td>
<td>334</td>
<td>949</td>
<td>126 (13.3%)</td>
<td>2.1 [1.5 – 3.0]</td>
<td>&lt; 0.001</td>
<td>2.2 [1.5 – 3.0]</td>
</tr>
</tbody>
</table>

The number of patients (No.) available for analysis is shown for each variable. The values shown are the numbers of patients (percentage). Adjusted analysis accounts for hypertension duration as a continuous variable. OR, odds ratio; CI, confidence interval. ³based on left ventricular mass index per unit body surface area (g/m²); ⁴left ventricular mass index >95 g/m² in women or >115 g/m² in men; ⁵relative wall thickness >0.42; ⁶relative wall thickness ≤0.42; ⁷based on left ventricular mass indexed for height².7 (g/m²²); ⁸left ventricular mass index >47 g/m²² in women or >50 g/m²² in men.