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Hypertension. 2006;48:239-245; originally published online June 19, 2006; doi: 10.1161/01.HYP.0000231338.41548.fc
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

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Plasma Aldosterone Is Independently Associated With the Metabolic Syndrome

Murielle Bochud, Jürg Nussberger, Pascal Bovet, Marc R. Maillard, Robert C. Elston, Fred Paccaud, Conrad Shamlaye, Michel Burnier

Abstract—The aim of this study was to analyze the associations of plasma aldosterone and plasma renin activity with the metabolic syndrome and each of its components. We analyzed data from a family based study in the Seychelles made up of 356 participants (160 men and 196 women) from 69 families of African descent. In multivariable models, plasma aldosterone was associated positively (P<0.05) with blood pressure in older individuals (interaction with age, P<0.05) and with waist circumference in men (interaction with sex, P<0.05) and negatively with high-density lipoprotein cholesterol, in particular in individuals with elevated urinary potassium excretion (interaction with urinary potassium, P<0.05); plasma renin activity was significantly associated with triglycerides and fasting blood glucose. Plasma aldosterone, but not plasma renin activity, was associated with the metabolic syndrome per se, independently of the association with its separate components. The observation that plasma renin activity was associated with some components of the metabolic syndrome, whereas plasma aldosterone was associated with other components of the metabolic syndrome, suggests different underlying mechanisms. These findings reinforce previous observations suggesting that aldosterone is associated with several cardiovascular risk factors and also suggest that aldosterone might contribute to the increased cardiovascular disease risk in individuals of African descent with the metabolic syndrome. (Hypertension. 2006;48:239-245.)

Key Words: aldosterone ■ metabolism ■ blood pressure ■ genetics

The metabolic syndrome (MS) represents a clustering of several cardiovascular risk factors, which include hypertension, dyslipidemia (low high-density lipoprotein [HDL] cholesterol and elevated triglycerides), abdominal obesity, glucose intolerance, and a proinflammatory and prothrombic state.1 The mechanisms linking these abnormalities are, however, not well understood.2 The MS is associated with increased cardiovascular morbidity and mortality,3–6 although the underlying mechanisms responsible for these associations are not yet fully known.7

The renin–angiotensin–aldosterone system plays a crucial role in blood pressure (BP) control, as well as in the progression of cardiovascular and renal diseases.8 A large body of evidence now suggests that aldosterone exerts cardiovascular effects that might go beyond the classically described kidney-mediated electrolyte and water homeostasis.9 In the last decades, much of the attention focused on the potentially deleterious effects of angiotensin II. However, recent observations have suggested that increased aldosterone levels are much more frequent in “essential” hypertension than thought previously.10–14 The Randomized ALdactone Evaluation Study (RALES)15 and Eplerenone Post-acutemyocardial infarction Heart failure Efficacy and SUrival Study (EPHESUS) trials16–17 have highlighted the key role of aldosterone in cardiovascular morbidity and mortality in patients with heart failure. Because both aldosterone and renin are associated with BP, and high BP is part of the MS, they may be associated independently with the MS in general and with specific components of it in particular.

Although the role of renin and aldosterone in BP regulation is well known, less is known about association of renin and aldosterone with the MS. Several observations suggest that plasma aldosterone (PA) plays a role in BP regulation in obesity.18–21 In addition, several studies have reported an association between aldosterone and/or plasma renin activity (PRA) and blood lipids22–24 and insulin resistance,22,25–27 which are components of the MS. Although Egan et al28 found that an activated renin–angiotensin–aldosterone system was associated with cardiovascular risk factor clustering, no association was found between the MS and aldosterone or PRA in a recent TROPHY substudy.27 The aim of this study was to analyze the association in an East African population of PA and PRA with: (1) the MS, and (2) each of its components.
Methods
The study took place in the Seychelles islands, which are populated predominantly by individuals of East African descent. Participants were recruited between August 1999 and January 2002. The selection process for families has been described previously.25 The protocol was accepted by the local ethical committee in Lausanne, Switzerland, and also accepted by the Ministry of Health of the Seychelles Islands. The main purpose of the study aimed at examining genetic determinants of hypertension within families including ≥2 hypertensive siblings. Therefore, we conducted these analyses post hoc. Patients treated with statins (n=4) were excluded. In addition, 134 individuals were excluded because data on hormones (n=54) or on one of the MS components (n=84) were not available. This study was composed of 356 individuals from 69 families.

We used a standard definition of the MS.1 The MS is defined for subjects with ≥3 of the following 4 factors: waist circumference >102 cm (40 in) in men and >88 cm (35 in) in women, triglycerides ≥150 mg/dL (1.69 mmol/L), HDL cholesterol <40 mg/dL (1.04 mmol/L) in men and <50 mg/dL (1.30 mmol/L) in women, office BP ≥130/85 mm Hg or on antihypertensive treatment, and fasting blood glucose ≥110 mg/dL (6.1 mmol/L) or on an antidiabetic agent.

Office BP was measured using a standard mercury sphygmomanometer with a cuff that automatically adapts the bladder to the arm circumference (TriCuff) in seated subjects who had been quiet for ≥10 minutes. The average of 3 readings was used for the definition of the MS. Antihypertensive therapy, if any, was stopped for 2 weeks before conducting ambulatory BP monitoring and measuring PRA and PA. Antihypertensive treatment was stopped in 149 participants for a median of 15 days (interquartile range, 12 to 22). Diuretics, angiotensin-converting enzyme (ACE) inhibitors, β-blockers, and calcium-channel blockers were stopped in, respectively, 73, 46, 42, and 65 participants. Ambulatory BP was measured using Diastar Integra devices (Novacor SA). Additional methodologic criteria have been described previously.26 For the analyses, we used the average of 10 randomly selected daytime BP measures to have the same number of measures for each participant. Body mass index (BMI) was calculated as weight (kilograms) divided by squared height (square meters). Waist was measured at the umbilicus level, on standing patients wearing only underwear, to the nearest 1 cm.

After an overnight fast, protocols began between 7:00 AM and 8:00 AM in a quiet room with the subject lying on a bed for 1 hour. Venous plasma was collected into prechilled glass tubes containing potassium EDTA and immediately centrifuged at 4°C. PRA was measured according to the antibody-trapping principle.31 We used high-affinity antibodies to protect angiotensin I generated in plasma against degradation during a 30-minute incubation at 37°C.32 The same antibodies after 100-fold dilution were subsequently used for radioimmunooassay.32 PA was measured by a direct radioimmunooassay using a very sensitive and specific antiserum raised in a New Zealand white rabbit.33 The coefficients of variation for within- and between- assay precision were 0.04 to 0.13 for the PRA and PA assays.32,33 The lower detection limits for PA and PRA were 2 pg/mL (5.548 pmol/L) and 0.05 ng/mL per hour (0.014 ng/Ls), respectively. PA and PRA are converted to SI units by multiplying 2.774 and 0.2778, respectively. For the analyses, we assumed the 26 samples below detection limit for PRA to have half the value of the detection limit. No participant was below the detection limit for PA.

Participants were given, on the same day as ambulatory BP monitoring was performed, plastic containers to collect urine for a 24-hour period under their usual diet. Urinary and plasma sodium and potassium concentrations were measured by flame photometry (IL-943, Instrumentation Laboratory). Fasting blood glucose was measured twice using a Glycotronic C reflectometer (Macherey-Nagel).

Statistical Methods
To compare data in participants with and without the MS, we obtained approximate P values (ie, not accounting for the correlated family data) using t tests for continuous and χ² tests for dichotomous variables. Spearman rank correlations were calculated between PA and PRA (after adjustment for age, sex, urinary sodium, and potassium) in participants with 0, 1, 2, 3, and >3 MS criteria. We used the ASSOC program in SAGE24 to conduct multiple linear regressions using centered continuous independent variables to avoid multicollinearity problems when adding interaction terms. ASSOC analyzes the association between a continuous trait and 1 or more covariates on the assumption that a power transformation of the trait leads to multivariate normality across pedigree members from pedigree data in the presence of familial correlations. Because this is a cross-sectional study and none of the variables can be considered to be measured with less error than the others, we conducted regression analyses both ways, that is, once using the MS components as the dependent variables and once using the hormones (PA and PRA) as the dependent variables. Regression coefficients and their SEs are presented on an untransformed scale. For independent observations, the following relationship relates the estimated regression coefficient b of Y on X to Pearson’s correlation coefficient r: b=r (sx, sy), where sx and sy represent the sample SDs of X and Y. No such simple relationship exists for correlated family data. All of the models included age and sex as covariates and were corrected for ascertainment as described previously.30 To analyze whether PA or PRA was associated with the entity MS, as defined by the National Cholesterol Education Program (NCEP) criteria,1 independent of the MS components, we added a variable (coded 1/0 for the presence/absence of MS) to a model containing all of the MS components. We repeated the analyses (1) after removing 26 individuals who were the most susceptible to having a primary aldosteronism (ie, those with hypertension [NCEP criteria] and both PA/PRA ratio and PA above the 75th percentile), and (2) adding BMI as a covariate.

Results
Participants’ characteristics are presented in Table 1. Most participants fulfilled the NCEP criteria for hypertension, which reflects the fact that families were ascertained on the

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Absent</th>
<th>Present</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>249</td>
<td>107</td>
<td>0.01</td>
</tr>
<tr>
<td>Age, y</td>
<td>45.0 (11.5)</td>
<td>48.5 (12.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>Sex, % women</td>
<td>50</td>
<td>67</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.0 (4.7)</td>
<td>31.2 (4.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Overweight (BMI ≥25), %</td>
<td>58</td>
<td>93</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Taken off treatment, %</td>
<td>36</td>
<td>56</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plasma aldosterone, pg/mL*</td>
<td>49 (20)</td>
<td>59 (27)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plasma renin activity, ng/L per hour*</td>
<td>0.33 (0.41)</td>
<td>0.44 (0.49)</td>
<td>0.17</td>
</tr>
<tr>
<td>Plasma potassium, mmol/L</td>
<td>3.8 (0.3)</td>
<td>3.7 (0.3)</td>
<td>0.60</td>
</tr>
<tr>
<td>Fasting blood glucose, mmol/L</td>
<td>4.4 (1.3)</td>
<td>5.8 (3.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.34 (0.35)</td>
<td>1.07 (0.26)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.0 (0.5)</td>
<td>1.6 (0.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>90 (12)</td>
<td>104 (10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Office hypertension, %</td>
<td>65</td>
<td>94</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Day systolic BP, mm Hg</td>
<td>129.5 (17.5)</td>
<td>135.0 (15.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>Day diastolic BP, mm Hg</td>
<td>84.1 (12.2)</td>
<td>85.7 (9.5)</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Results are means (SD) unless specified otherwise. MS was defined using National Cholesterol Education Adult Treatment Panel III criteria. *Results are medians (interquartile range).

Hypertension, defined as office BP ≥130/85 mm Hg or on antihypertensive treatment.
basis of the presence of ≥2 hypertensive siblings. PA was significantly higher, and PRA tended to be higher, in participants with than without the MS. Figure 1 illustrates the rightward shift in distribution of PA, but not PRA, in participants with, as compared with those without, the MS. PA tended to increase, and the positive correlation between PA and PRA tended to decrease, with an increasing number of MS risk factors (Figure 2). After removing participants with any suspicion of primary aldosteronism, the rank correlations between PA and PRA were, for participants with, respectively, 0, 1, 2, 3, and ≥3 MS components, 0.32 (n=29; \( P=0.09 \)), 0.27 (n=93; \( P=0.008 \)), 0.13 (n=114; \( P=0.16 \)), 0.17 (n=55; \( P=0.22 \)), and 0.17 (n=39; \( P=0.30 \)). The near 0 correlation between PA and PRA in participants with the MS may, therefore, be, in part, because of primary aldosteronism.

Table 2 presents regression coefficients of components of the MS on hormones. PA was significantly associated with all components of the MS except for fasting blood glucose. In contrast, PRA was significantly associated with only triglycerides and fasting blood glucose. The different associations

![Figure 1. Distribution of PA and PRA. A and B, Distributions of PA and PRA in the whole sample (N=356). C and D, Distribution according to the presence ( ) or the absence ( ) of MS.](http://hyper.ahajournals.org/)

![Figure 2. PA and PRA by number of metabolic risk factors. Results are medians and interquartile ranges. Solid lines and ■ represent PA. Dashed lines and □ represent PRA. P (trend) is the \( P \) value for a nonparametric test for trend, \( P \) (median) is the \( P \) value for a test of equal medians across all categories. \( r \) is the Spearman rank correlation between PA and PRA levels within each category. Na/K represents the 24-hour urinary sodium/potassium excretion, expressed in mmol/24 hour.](http://hyper.ahajournals.org/)
further suggest that the association of PA with the MS is independent of PRA. No significant interaction between PRA and any of the covariates used in the models was found. In contrast, a positive linear trend between PA and BP was only observed among older participants; a positive linear trend between PA and waist was only observed in men and increased with increasing urinary potassium excretion; the association between PA and HDL became more negative with increasing urinary potassium excretion (see also Figure 3). Analyses without participants with a suspicion of primary aldosteron-

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**TABLE 2. Regression Coefficients of Components of the MS on PA and PRA and Their Significant Interactions**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Type of Analysis</th>
<th>Day SBP, mm Hg</th>
<th>Day DBP, mm Hg</th>
<th>Waist, cm</th>
<th>HDL, mmol/L</th>
<th>Triglycerides, mmol/L</th>
<th>FBG, mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td>Model A Main effect</td>
<td>-0.02 (0.04)</td>
<td>0.007 (0.03)</td>
<td>0.14 (0.04)</td>
<td>-0.003 (0.001)</td>
<td>0.003 (0.001)</td>
<td>0.004 (0.004)</td>
</tr>
<tr>
<td></td>
<td>Interaction</td>
<td>0.007 (0.003)†</td>
<td>0.007 (0.002)*</td>
<td>-0.18 (0.06)*</td>
<td>(PA \times \text{age})</td>
<td>(PA \times \text{sex})</td>
<td>(PA \times \text{sex})</td>
</tr>
<tr>
<td></td>
<td>Model B Main effect</td>
<td>-0.005 (0.04)</td>
<td>0.012 (0.027)</td>
<td>0.16 (0.04)</td>
<td>-0.003 (0.001)</td>
<td>0.004 (0.001)*</td>
<td>0.005 (0.003)</td>
</tr>
<tr>
<td></td>
<td>Interaction</td>
<td>0.006 (0.003)†</td>
<td>0.007 (0.002)*</td>
<td>-0.17 (0.06)*</td>
<td>(PA \times \text{sex})</td>
<td>(PA \times \text{sex})</td>
<td>(PA \times \text{urine K})</td>
</tr>
<tr>
<td></td>
<td>Interaction</td>
<td>0.004 (0.002)†</td>
<td>(PA \times \text{urine K})</td>
<td>(PA \times \text{urine K})</td>
<td>(PA \times \text{urine K})</td>
<td>(PA \times \text{urine K})</td>
<td>(PA \times \text{urine K})</td>
</tr>
<tr>
<td>PRA</td>
<td>Model A Main effect</td>
<td>2.49 (2.03)</td>
<td>1.00 (1.39)</td>
<td>1.47 (1.65)</td>
<td>-0.01 (0.04)</td>
<td>0.13 (0.07)</td>
<td>0.34 (0.18)</td>
</tr>
<tr>
<td></td>
<td>Model B Main effect</td>
<td>2.95 (1.98)</td>
<td>1.12 (1.38)</td>
<td>1.96 (1.64)</td>
<td>-0.03 (0.04)</td>
<td>0.13 (0.07)†</td>
<td>0.36 (0.18)†</td>
</tr>
</tbody>
</table>

This table presents regression coefficients (SE) for the main effects of PA and PRA and their interactions with other covariates from 24 models. Dependent variables are the components of the MS. Continuous predictors were mean centered. In addition to PA or PRA, models A included age, sex, ascertainment, and their significant 2-way interactions as covariates. In models B, urine sodium and potassium and plasma potassium were added as covariates (also including significant 2-way interactions). Only significant interactions with PA or PRA are reported in the table. SBP/DBP indicates systolic/diastolic daytime ambulatory blood pressure; FBG, fasting blood glucose.

* \(P<0.01\); † 0.01 < \(P<0.05\).
Discussion

These results demonstrate that MS is independently associated with aldosterone levels (ie, PA levels are 20% higher in the presence versus the absence of the MS), independent of the MS components. This is not because of only a few MS individuals with elevated PA, because the whole PA distribution is shifted to the right in those with the MS. This finding is highly relevant in view of: (1) the increased mortality associated with the MS, (2) the potential role of aldosterone in the development of cardiovascular complications, and (3) the high prevalence of hypertension (40%) and MS (22%) in the general Seychelles population. El-Gharbawy et al found a positive association between aldosterone and left-ventricular hypertrophy in obese hypertensive blacks who had similar aldosterone values as those found in our study. We, therefore, consider the magnitude of the observed effect, although modest at the individual level, to potentially represent a substantial burden at the population level.

So far only 1 study has reported increased aldosterone in patients with a clustering of cardiovascular risk factors. That study, which included 29 volunteers of unidentified ethnicity, also found increased PRA, in particular under a low-salt diet. In a recent TROPHY substudy, no evidence for elevated aldosterone or PRA was found in subjects with the MS when compared with controls without the syndrome. That study, however, included mostly white participants and the results may, therefore, not apply to individuals of African descent.

The fact that PA and PRA were less correlated in participants with the MS and were associated differently with components of the MS suggest that these factors are related to the MS, at least in part, through independent mechanisms. The control of aldosterone secretion is complex. Although angiotensin II represents a major regulator of aldosterone, recent evidence from clinical trials underscores the role of aldosterone even in the presence of a blunted renin–angiotensin system. For instance,
mineralocorticoid receptor blockade (spironolactone) further lowers BP in type 2 diabetic patients with nephropathy already treated with ACE inhibitors and angiotensin II receptor blockers (ARBs). In the RALES15 and EPHEBUS16 trials, spironolactone and eplerenone (2 aldosterone receptor blockers) significantly reduced all-cause and cardiovascular mortality compared with placebo when added to standard therapy.

In our study, which included 66% overweight participants, only PA, but not PRA, was significantly associated with daytime ambulatory BP. We found a significant interaction with age that showed aldosterone to be positively associated with BP only in older participants. Similarly, Grim et al18 found that aldosterone, but not PRA, correlated positively with BP in individuals of African descent. In the latter study,38 the correlation between BP and aldosterone was much stronger in blacks than in whites. El-Gharbawy et al36 had shown previously that a positive correlation between aldosterone and BP in blacks was significant only among obese individuals. The selective aldosterone blocker eplerenone effectively lowered BP in black and white hypertensive patients90 but was more effective than losartan only in blacks. These observations give further credence to the role of aldosterone in BP control, specifically in subjects of African descent.

We found that PA and PRA were negatively associated with HDL cholesterol, independent of all other MS components. This is consistent with previous reports.22–24 Recently, Gaudio et al40 found HDL cholesterol to increase in response to a combination therapy of an ACE inhibitor and an ARB, which provides experimental evidence that the renin–angiotensin–aldosterone system interacts with lipid metabolism in humans. We have now demonstrated that these associations can also be found in individuals of African descent.

In our study PRA, but not aldosterone, was associated with fasting blood glucose. Although we did not measure insulin resistance, our results are consistent with previous observations showing an association between PRA and insulin resistance.26–27,41 Lind et al26 found that insulin resistance was associated more strongly with PRA than aldosterone. Haenni et al41 found an increase in PRA, but not aldosterone, during a euglycemic hyperinsulinemic clamp test in 49 hypertensive patients. In a recent meta-analysis,42 ARB and ACE inhibitors seemed to decrease the incidence of diabetes mellitus by \( \approx 20\% \) when compared with placebo, \( \beta \)-blockers, diuretics, or amloidipine. These findings would also suggest that the renin–angiotensin system is related to glucose intolerance independent of BP control.

Findings from in vitro studies provide some insight as to which mechanisms might explain the relationships between metabolic disturbances and the renin–angiotensin–aldosterone system. Human fat is now recognized to be a highly active endocrine tissue. It has been postulated that visceral fat might affect adrenal steroidogenesis.19 Goodfriend et al43 observed that an oxidized derivative of linoleic acid, a fatty acid that is increased in obesity, stimulated aldosterone secretion by rat adrenal cells and correlated positively with PA and BP in humans. Ehrhart-Bornstein et al44 have shown that some (as yet unidentified) products secreted by adipocytes directly stimulate the secretion of aldosterone by human adrenocortical cells. Other potential links between the renin–angiotensin system and the MS point to plasma leptin45 and adiponectin.46

Our study has some limitations. Participants came from families with a history of hypertension: this common background clearly limits the generalizability of our results to the general population. However, because we also recruited family members with normal BP, the full BP range was represented. Furthermore, we corrected our models for ascertainment (ie, for the fact that recruitment was constrained to include 2 hypertensive siblings in each family). Such a correction aims to determine what would have been the results had the participants not been ascertained this way. This correction results in a better generalizability of our observations.79

Perspectives

We report that aldosterone, but not PRA, is associated with the MS, even after adjusting for all of its separate components, which would indicate that the clustering of these factors per se is associated with aldosterone. Although an association does not necessarily imply a cause-effect relationship, this finding suggests that aldosterone might contribute to the increased cardiovascular disease risk in individuals of African descent with the MS. So far, there is no evidence that specific aldosterone blockade favorably impacts the clinical course of patients with the MS and/or is superior to other antihypertensive medications, but these hypotheses would be worth testing experimentally.

Acknowledgments

We thank the Ministry of Health and Social Services of the Republic of Seychelles for their support of this epidemiological research, and Air Seychelles and SkyChef for their logistic support in transporting equipment and samples.

Sources of Funding

The study benefited from a grant from the Swiss National Science Foundation (TANDEM No 31-51115.97) and from the Faculty of Biology and Medicine of Lausanne, Switzerland. It was also supported in part by a US Public Health Service Resource grant (RR03655) from the National Center for Research Resources and Research grant (GM28356) from the National Institute of General Medical Sciences.

Disclosures

None.

References

5. Ford ES. The metabolic syndrome and mortality from cardiovascular disease and all-causes: findings from the National Health and Nutrition
10. Vasan RS, Evans JC, Larson MG, Wilson PWF, Meigs JB, Rifai N, Benjamin EJ, Levy D. Serum aldosterone and the incidence of hyper-
cardial Infarction Heart Failure Efficacy and Survival Study Investigators. Eplerenone, a selective aldosterone blocker, in patients with left ventric-