Renin-Angiotensin System

Urinary Angiotensinogen Excretion Is Associated With Blood Pressure Independent of the Circulating Renin–Angiotensin System in a Group of African Ancestry

Frederic S. Michel,* Gavin R. Norton,* Muzzi J. Maseko, Olebogeng H.I. Majane, Pinhas Sareli, Angela J. Woodiwiss*

Abstract—Although the circulating renin–angiotensin system (RAS) is suppressed in salt-sensitive populations, the role of the intrarenal RAS in blood pressure (BP) control in these groups independent of the circulating RAS is uncertain. We evaluated the relationship between 24-hour urinary angiotensinogen excretion and either office (mean of 5 measurements; n=425) or 24-hour ambulatory (n=340) BP independent of the circulating RAS in a community-based sample of African descent that had never received antihypertensive drug therapy. Circulating RAS activity was determined from plasma renin and angiotensinogen and serum aldosterone concentrations. Urinary angiotensinogen to creatinine ratio (angiotensinogen/creat) was correlated with plasma angiotensinogen concentrations (P<0.0005) but not with indexes of salt intake. However, urinary angiotensinogen/creat was independently associated with office systolic BP (partial r=0.16; P<0.001), whereas plasma angiotensinogen (partial r=0.07; P=0.14) was not independently associated with office systolic BP. Urinary angiotensinogen/creat was also associated with 24-hour systolic BP (partial r=0.11; P<0.05). The relationships between urinary angiotensinogen/creat and BP survived further adjustments for plasma angiotensinogen and serum aldosterone concentrations, plasma renin concentrations, estimated glomerular filtration rate, urinary Na+/K+, or 24-hour urinary Na+ excretion rates (P<0.005 for all). Participants with the highest compared with the lowest quartile of urinary angiotensinogen/creat showed an 8.2-mmHg higher office (P<0.005) and 4.6-mmHg higher 24-hour (P=0.01) systolic BP. In conclusion, independent of the systemic RAS, including plasma angiotensinogen concentrations, urinary angiotensinogen excretion is associated with BP in a salt-sensitive, low-renin group of African descent. These data lend further support for a role of the RAS in BP control in salt-sensitive groups of African ancestry. (Hypertension. 2014;64:149-156.)

Key Words: African Continental Ancestry Group ■ blood pressure monitoring, ambulatory ■ renin–angiotensin system ■ urine angiotensinogen

In salt-sensitive populations, such as those of African ancestry, a high-sodium (Na+), low-potassium (K+) diet results in renal Na+ retention and increases in blood pressure (BP).1,2 As a consequence of an enhanced Na+ retention, renin release from the juxtaglomerular apparatus decreases and the activity of the systemic renin–angiotensin system (RAS) is suppressed.3–6 Thus, the effect of RAS blockers on BP in salt-sensitive populations such as those of African ancestry is limited,7,8 and RAS blockers are not recommended as first-line therapy in these populations.9,10 However, there is ongoing debate as to the role of the RAS in salt-sensitive hypertension, particularly in groups of African ancestry.

In addition to the systemic RAS, a complete local intrarenal RAS exists.11,12 In angiotensin II–induced hypertension, augmentation of intrarenal angiotensinogen mediates intrarenal angiotensin II production.13–15 Because urinary angiotensinogen is derived largely from proximal tubular angiotensinogen, urinary angiotensinogen excretion is a biomarker of intrarenal RAS activity.16,17 Although associations between urinary angiotensinogen excretion and BP have previously been described,18–21 these relationships in typical salt-sensitive groups of African ancestry have been reported on in only 12 black African men.20 Because intrarenal RAS activation depends on the activity of the systemic RAS11,12 and the systemic RAS is suppressed in groups of black African descent,1–6,10 one would not predict an important role for the intrarenal RAS in BP control in this ethnic group. However, to what extent the effect of the intrarenal RAS on BP depends on the systemic RAS is uncertain. Whether relationships between urinary angiotensinogen excretion and BP are better than the well-recognized relationships between plasma angiotensinogen concentrations22–24 or the circulating RAS25–29 and BP has not been reported.18–21 Because the role of the intrarenal RAS in BP control in communities characterized by a
low circulating RAS, such as in groups of African ancestry, is unknown, in the present study, we evaluated whether urinary angiotensinogen excretion is associated with BP, independent of the systemic RAS in a group of South Africans of African ancestry.

Methods

Study Group

The present study was conducted according to the principles outlined in the Helsinki declaration. The Committee for Research on Human Subjects of the University of the Witwatersrand approved the protocol (approval number: M02-04-72 and renewed as M07-04-69 and M12-04-108). Participants gave informed, written consent. The study design has previously been described.24,29,30 Briefly, 425 participants of black African descent ≥16 years of age with 24-hour urine samples who met with prespecified quality control criteria previously described24,29,30 and who had never received antihypertensive drug therapy were randomly recruited from the South West Township of Johannesburg, South Africa. Of these participants, 340 had 24-hour ambulatory BP monitoring that met with the European Society of Hypertension guidelines (>14 and 7 readings for the computation of day and night means, respectively).31

Clinical, Demographic, and Anthropometric Measurements

A standardized questionnaire was administered to obtain demographic and clinical data.24,29,30 From height and weight measurements, body mass index (BMI) was calculated and participants were identified as being overweight if their BMI was ≥25 kg/m² and obese if their BMI was ≥30 kg/m². Standard laboratory blood and urine tests were performed. Diabetes mellitus or abnormal blood glucose control was defined as the use of insulin or oral hypoglycemic agents or an hemoglobin A1c >6.1%. Estimated glomerular filtration rate was determined using the abbreviated Modification of Diet in Renal Disease study group equation: 186.3×(serum creatinine in mg/dL⁻¹.154)×(age in years⁻⁰.203)×1.212×0.742 (if woman).

Blood Pressure

Nurse-derived conventional BP was measured after 10 minutes of rest in the seated position as previously described24,29,30 within a half hour of obtaining blood samples in the opposite arm to that subjected to venesection. Five consecutive BP readings were obtained using an appropriately sized cuff, 30 to 60 seconds apart. The average of the 5 readings was taken as the BP. Only 0.23% of visits had fewer than 5 readings was the BP. Only 0.23% of visits had fewer than 5 readings. The frequency of identical consecutive readings was 0.23% for systolic BP (SBP) and 0.94% for diastolic BP (DBP). The average of 24-hour, day, and night BP were determined using SpaceLabs monitors (model 90207; Spacelabs, Redmond, WA) as previously described.30 The size of the cuff was the same as that used for conventional BP measurements. Monitors were programmed to measure 24-hour BP at 5-minute intervals from 06:00 to 22:00 hours and at 30-minute intervals from 22:00 to 06:00 hours. Fixed-clock time periods, identified as previously described,30 rather than actual in bed and out of bed periods were statistically analyzed to ensure that similar day and nighttime periods were selected for comparisons between individuals. Day and night periods ranged from 09:00 to 19:00 hours and from 23:00 to 05:00 hours, respectively.

No participants reported on daytime naps. Intraindividual means of the ambulatory measurements were weighted by the time interval between successive readings.30 The average (±SD) number of BP readings obtained was 62.1±11.6 (range, 25–81) for the 24-hour period, 29.1±7.0 (range, 14–41) for the day, and 9.4±1.0 (range, 7–11) for the night periods. Exclusion of readings obtained during the transition periods resulted in a lower number of readings for the day and night periods combined compared with the total obtained for the 24-hour period.

Circulating Renin, Aldosterone, and Angiotensinogen Concentrations

Blood samples were obtained in the supine position after 10 minutes of rest in the morning between 10:00 and 12:00 hours. After centrifugation, samples were stored at −70°C until the time of analysis. Plasma renin concentrations were measured using an immunoradiometric technique (Renin III Generation, Cisbio International, Ceze, France; intra-assay coefficients of variation ranging from 1.1% for high concentrations to 4.5% for low concentrations and with a mean interassay coefficient of variation of 5.3%). Serum aldosterone concentrations were measured using an ¹²⁵I radioimmunoassay (Coat-A-Count, Diagnostic Products Corporation, Los Angeles, CA; intra-assay coefficients of variation ranging from 2.3% for high concentrations to 5.4% for low concentrations and with a mean interassay coefficient of variation of 5.4%). Plasma angiotensinogen concentrations were determined using a human total angiotensinogen solid phase sandwich ELISA (code No. 27412, Immuno-Biological Laboratories, Co, Ltd, Gunma, Japan; intra-assay coefficients of variation ranging from 4.4% for high concentrations to 5.5% for low concentrations and with an interassay coefficient of variation ranging from 4.3% for high concentrations to 7.0% for low concentrations).

Urine Measurements

Timed urine samples were obtained for a 24-hour period after discarding urine obtained immediately before the start of the collection period. The mean (±SD) time period of urine collection was 24.5±1.5 hours (range, 24.0–31.1 hours). The quality of urine sample collection was determined as previously described.24,29,30 Urinary Na⁺, K⁺, and creatinine concentrations were measured and 24-hour urine Na⁺ excretion rates calculated from the product of 24-hour urine volumes and urine Na⁺ concentrations. Urinary angiotensinogen concentrations were determined using the same human total angiotensinogen solid phase sandwich ELISA (code No. 27412, Immuno-Biological Laboratories, Co, Ltd, Gunma, Japan) as that used to determine plasma angiotensinogen concentrations. Urine angiotensinogen excretion rates were expressed as angiotensinogen to creatinine ratio (angiotensinogen/creat).

Data Analysis

For database management and statistical analysis, SAS software, version 9.3 (SAS Institute Inc, Cary, NC), was used. Data are shown as mean±SD unless otherwise specified. Proportions were compared by the χ² statistic. Because circulating renin, aldosterone, and angiotensinogen concentrations were not normally distributed, in data analysis they were expressed as log renin, square root aldosterone, and square root angiotensinogen values. Because urine angiotensinogen excretion rates and urinary Na⁺/K⁺ were also not normally distributed, they were expressed as log urinary angiotensinogen/creat ratio and log urinary Na⁺/K⁺. Relationships between urinary angiotensinogen excretion rates and BP were determined from multivariate regression models with age, sex, BMI, the presence of diabetes mellitus/abnormal blood glucose control, regular alcohol consumption, and regular tobacco use included in the regression models. The probability values derived from multivariate models were adjusted for nonindependence of family members using a mixed model of analysis as defined by SAS software. Because estrogen influences angiotensinogen expression and angiotensinogen is expressed in adipose tissue, we also evaluated whether interactions between sex or BMI and urinary angiotensinogen/creat ratios are associated with BP.

Results

Characteristics of the Participants

Table 1 shows the characteristics of the study sample and of participants of the study sample who had 24-hour BP data that met with prespecified quality control criteria. More women than men participated. A high proportion of participants had hypertension that had never been treated with antihypertensive drugs (24.2%).
Factors Independently Associated With Urinary Angiotensinogen Excretion

In a multivariate model, plasma angiotensinogen concentrations were positively associated with the urinary angiotensinogen/creat (Table 2), and urinary angiotensinogen/creat increased across quartiles of plasma angiotensinogen concentrations (Figure 1). However, neither plasma renin nor serum aldosterone concentrations, estimated glomerular filtration rate, or indexes of salt intake (24-hour urinary Na+ excretion or Na+/K−; Table 2) were correlated with urinary angiotensinogen/creat. Moreover, no differences in urinary angiotensinogen/creat were noted across quartiles of urinary Na+/K−, an index of salt intake (Figure 1), or 24-hour urinary Na+ (data not shown).

Relationships Between Circulating or Urinary RAS Activity and BP

In keeping with a salt-sensitive population, plasma renin concentrations were inversely associated with office and 24-hour SBP (Table 3), and both office (Figure 2) and 24-hour (Figure 3) SBP decreased across quartiles of plasma renin concentrations. Neither plasma angiotensinogen nor serum aldosterone concentrations were associated with either office or 24-hour BP (Table 3; Figures 2 and 3). However, urinary angiotensinogen/creat was independently associated with office and 24-hour SBP, and office or 24-hour SBP increased across quartiles of urinary angiotensinogen/creat (Table 3; Figures 2 and 3). An 8.2-mm Hg greater office and 4.6-mm Hg 24-hour SBP was noted in the highest compared with the lowest quartile of urinary angiotensinogen/creat (Figures 2 and 3). The relationships between urinary angiotensinogen/creat and office or 24-hour SBP were not to be independent of the circulating RAS, including plasma angiotensinogen concentrations, as well as of indexes of salt intake (urinary Na+/K− and 24-hour urinary Na+ excretion; Table 4).

Dependence of the Relationship Between Urinary Angiotensinogen and BP on Na+ Intake, Sex, or BMI

No positive interaction between urinary angiotensinogen/creat and 24-hour urinary Na+ excretion or urinary Na+/K− (indexes of Na+ intake) was associated with either office or 24-hour SBP (data not shown). Moreover, no interactions between urinary angiotensinogen/creat and sex or BMI were associated with either office or 24-hour SBP (data not shown).

Table 2. Factors Independently Associated With Urinary Angiotensinogen Excretion in a Group of African Ancestry Never Having Received Antihypertensive Therapy (n=425)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With 24-h BP Data</th>
<th>CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Urinary Angiotensinogen/Creatinine vs Partial r (CI)</td>
<td>0.17 (0.08 to 0.26)</td>
<td>0.0005</td>
<td></td>
</tr>
<tr>
<td>Log plasma renin</td>
<td>−0.03 (−0.12 to 0.07)</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Log square root serum aldosterone</td>
<td>−0.003 (−0.10 to 0.09)</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>Log 24-hour urinary Na+</td>
<td>−0.07 (−0.16 to 0.03)</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>Log urinary Na+/K−</td>
<td>0.08 (−0.01 to 0.18)</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>0.07 (−0.02 to 0.17)</td>
<td>0.13</td>
<td></td>
</tr>
</tbody>
</table>

CI indicates confidence interval; GFR, glomerular filtration rate; K−, potassium; and Na+, sodium.

*With adjustments for age, sex, body mass index, diabetes mellitus or an hemoglobin A1c>6.1%, regular tobacco use, and regular alcohol consumption. Probability values are further adjusted for nonindependence of family members.
In the present study, we explored the relationship between urinary angiotensinogen excretion and BP in a community sample of African ancestry (none of whom had received antihypertensive drug therapy) with typical salt sensitivity (as indexed by strong inverse relationships between plasma renin concentrations and both BP and urinary Na+/K+). In this regard, despite a lack of positive association between the systemic RAS and BP, urinary angiotensinogen excretion (angiotensinogen/creatinine) was independently associated with both office and 24-hour SBP. Moreover, relationships between urinary angiotensinogen/creatinine and BP were independent of circulating angiotensinogen, renin, and aldosterone concentrations, as well as of indexes of Na+ intake.

The results of the present study provide the first evidence to show in a relatively large, randomly selected study sample that urinary angiotensinogen/creatinine is associated with BP in a group of black African descent with typical salt sensitivity (inverse relationships between plasma renin concentrations and both BP and an index of salt intake). In this regard, relationships between urinary angiotensinogen/creatinine and BP in groups of African ancestry have previously been demonstrated in only 12 selected black men20 and in a small study sample (n=106) consisting of a combination of selected white, Asian, and blacks, only 56 of whom were black.19 The present findings, therefore, lend support for the previously suggested notion that despite poor BP responses to RAS blocker monotherapy7,8 and inverse relationships between Na+ intake and circulating RAS concentrations and between plasma renin concentrations and BP in groups of African ancestry, the renal RAS may play an important role in BP regulation in this ethnic group.24

Although in the present study we demonstrated relationships between urinary angiotensinogen/creatinine and BP but not 24-hour urinary Na+ excretion, in a prior study21 relationships between urinary angiotensinogen/creatinine and both BP and 24-hour urinary Na+ excretion were noted. In this regard, the authors of this prior study21 suggested that these relationships indicated a role for the intrarenal RAS in mediating salt-sensitive hypertension, a conclusion not supported by the present study. An explanation for the discrepancies between studies is that previously reported21 relationships between urinary angiotensinogen/creatinine and 24-hour urinary Na+ excretion were over a range of 24-hour urinary Na+ excretion values that

![Figure 1](https://hyper.ahajournals.org/)

**Table 3.** Independent Relationships Between Circulating or Renal Indices of RAS Activity and BP in a Group of African Ancestry Never Having Received Antihypertensive Therapy

<table>
<thead>
<tr>
<th>Indices of RAS Activity</th>
<th>Office BP (n=425)</th>
<th>24-h BP (n=340)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Partial r (Cl)</td>
<td>P Value</td>
</tr>
<tr>
<td>Systolic BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log plasma renin</td>
<td>−0.21 (−0.30 to −0.12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Square root serum aldosterone</td>
<td>0.01 (−0.09 to 0.11)</td>
<td>0.85</td>
</tr>
<tr>
<td>Square root plasma angiotensinogen</td>
<td>0.07 (−0.02 to 0.17)</td>
<td>0.14</td>
</tr>
<tr>
<td>Log urinary angiotensinogen/creatinine</td>
<td>0.16 (0.07 to 0.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log plasma renin</td>
<td>−0.24 (−0.33 to −0.15)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Square root serum aldosterone</td>
<td>−0.02 (−0.12 to 0.07)</td>
<td>0.64</td>
</tr>
<tr>
<td>Square root plasma angiotensinogen</td>
<td>0.08 (−0.02 to 0.17)</td>
<td>0.11</td>
</tr>
<tr>
<td>Log urinary angiotensinogen/creatinine</td>
<td>0.06 (−0.04 to 0.16)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; Cl, confidence intervals; and RAS, renin–angiotensin system. *With adjustments for age, sex, body mass index, diabetes mellitus or a hemoglobin A1c>6.1%, regular tobacco use, and regular alcohol consumption. Probability values are further adjusted for nonindependence of family members.
by far exceeded the maximal Na⁺ consumption in the present community sample. Yet, in the present study, relationships between urinary angiotensinogen/creat and BP were still noted. Importantly, whether Na⁺ intake has an effect on urinary angiotensinogen and whether intrarenal angiotensinogen contributes toward salt-sensitive hypertension remains controversial. Intrarenal or urinary angiotensinogen may increase or renal angiotensinogen mRNA levels may decrease with a high salt load. Moreover, in transgenic mice models, overexpression of proximal tubular angiotensinogen causes hypertension regardless of salt intake, whereas overexpression of liver angiotensinogen causes salt-sensitive hypertension. Despite inconsistencies in the ability to show relationships between urinary angiotensinogen/creat and 24-hour urinary Na⁺ intake in the present and a prior study, in both studies relationships between urinary angiotensinogen/creat and BP remained after further adjustments for indexes of Na⁺ intake.

Although several studies have demonstrated that urinary angiotensinogen/creat is associated with BP in white or Asian samples, whether these relationships are better than or independent of the previously described relationships between plasma angiotensinogen concentrations and BP is uncertain. In the present study, we show associations between urinary angiotensinogen/creat and BP, whereas no significant relationships between plasma angiotensinogen and BP were noted, despite a relationship observed between plasma angiotensinogen concentrations and urinary angiotensinogen/creat. Importantly, the urinary angiotensinogen excretion–BP relationships were noted in a typically salt-sensitive group where plasma renin concentrations were inversely correlated with BP. In keeping with one prior study, we also show that the associations between urinary angiotensinogen/creat and BP persisted with adjustments for plasma angiotensinogen concentrations. Moreover, despite relationships noted between urinary angiotensinogen/creat and BP in the present study, no relationships between serum aldosterone concentrations and BP were noted, and relationships between urinary angiotensinogen/creat and BP were independent of circulating aldosterone concentrations.

Hence, in the present study, associations between renal RAS activity, as indexed by urinary angiotensinogen/creat and BP, were independent of indexes of the systemic RAS.

In the present study, plasma angiotensinogen concentrations were correlated with urinary angiotensinogen excretion, a finding that is likely to be explained by augmentation of intrarenal angiotensinogen production by the extrarenal RAS, rather than by filtration of angiotensinogen at the glomerulus. Because of its molecular size (50–60 kDa), little angiotensinogen is expected to cross the glomerular membrane and systemic infusion of angiotensinogen does not result in detectable angiotensinogen in the urine. Consistent with this notion, in...
In the present study, we show no relationship between urinary angiotensinogen excretion and estimated glomerular filtration rate. Although circulating angiotensinogen concentrations were correlated with urinary angiotensinogen/creatin, urinary angiotensinogen excretion, but not plasma angiotensinogen concentrations, was associated with BP. This may reflect the more important role of the renal as opposed to the systemic RAS in BP control over the relatively low range of Na+ intake values observed in the present population. As we have previously reported, it is nevertheless possible that at a higher Na+ intake, systemic rather than renal angiotensinogen plays a more important role in BP control.

Although speculative, the clinical implications of the present study warrant consideration. In this regard, although the effect of RAS blockers on BP in salt-sensitive populations such as those of African ancestry are limited, the present results suggest that irrespective of a suppressed systemic RAS, the intrarenal RAS may play an important role in BP regulation in a proportion of these individuals. Hence, in contrast to the recommendations by some guidelines that RAS blockers should not be first-line therapy in black African populations, targeting the renal RAS may be an important therapeutic approach in a subgroup of these patients even in the presence of systemic RAS suppression. Further studies are, therefore, required to evaluate whether RAS blockers produce enhanced antihypertensive effects in groups of African descent with increased urinary angiotensinogen excretion rates.

Table 4. Relationships Between Urinary Angiotensinogen Excretion and Office SBP in a Group of African Ancestry Never Having Received Antihypertensive Therapy, With Adjustments for Measures of the Circulating RAS, Na+ Intake, or GFR

<table>
<thead>
<tr>
<th>Adjustments</th>
<th>Partial r* (CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log urinary angiotensinogen/creatinine vs office SBP (n=425)</td>
<td>0.15 (0.06–0.24)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>*and Log plasma renin</td>
<td>0.16 (0.06–0.25)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>*and Log plasma aldosterone</td>
<td>0.16 (0.06–0.25)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>*and Log 24-h urinary Na+</td>
<td>0.16 (0.07–0.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>*and Log urinary Na+/K+</td>
<td>0.15 (0.06–0.25)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>*and Estimated GFR</td>
<td>0.16 (0.06–0.25)</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

Cl indicates confidence intervals; GFR, glomerular filtration rate; K+, potassium; Na+, sodium; RAS, renin–angiotensin system; and SBP, systolic blood pressure.

*Adjustments are for age, sex, body mass index, diabetes mellitus or an hemoglobin A1c>6.1%, regular tobacco use, regular alcohol consumption and circulating measure of RAS, indexes of Na+ intake, or estimated GFR as indicated. Probability values are further adjusted for nonindependence of family members.

Figure 3. Multivariate-adjusted 24-hour systolic blood pressure across quartiles of circulating concentrations of renin, angiotensinogen (AGT), and aldosterone or urinary angiotensinogen excretion (log urinary AGT/creatinine) in a group of African ancestry. *P=0.01, **P<0.005 vs quartile 1; †P=0.01 vs quartile 2. Adjustments are for age, sex, body mass index, diabetes mellitus or an hemoglobin A1c>6.1%, regular tobacco use, and regular alcohol consumption. Probability values are further adjusted for nonindependence of family members.
that the independent relationships between urinary angiotensinogen excretion and BP reflect reverse causality, where as a compensatory response to an elevated BP, and after a reduced renin release, less renal angiotensinogen is converted to angiotensin II and hence more appears in the urine. However, the relationships noted between urinary angiotensinogen and BP in the present study were independent of plasma renin concentrations, despite the strong inverse relationships between plasma renin concentrations and BP. Moreover, plasma renin concentrations were not associated with urinary angiotensinogen excretion. Second, a high proportion of participants were women and obese, and we were not statistically powered to perform sex-specific analysis or analysis in categories of obesity. Thus, the relationships noted may relate specifically to women or obese individuals only.

Perspectives
The role of the RAS in salt-sensitive populations, such as those of African ancestry, is currently uncertain. In the present study, we show in a group of South Africans of African ancestry having never received antihypertensive therapy that despite strong inverse relationships between plasma renin concentrations and BP and a lack of relationship between circulating angiotensinogen or aldosterone concentrations and BP, urinary angiotensinogen excretion, as indexed by urinary angiotensinogen/creatin, is associated with both office and 24-hour BP. Importantly, these relationships were independent of urinary indexes of Na\(^+\) intake and of the circulating RAS. The present study, therefore, provides evidence to suggest that in salt-sensitive groups of African ancestry, despite suppression of the circulating RAS, the intrarenal RAS may contribute toward BP control and that this effect is independent of both Na\(^+\) intake and the circulating RAS.

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Disclosures
None.

References


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**Novelty and Significance**

**What Is New?**

- The role of the intrarenal renin–angiotensin system (RAS), independent of the systemic RAS, in blood pressure (BP) control in salt-sensitive, low-renin groups of African ancestry is unknown.

**What Is Relevant?**

- Because the systemic RAS is suppressed in salt-sensitive groups of African ancestry, RAS blockers are not recommended as first-line therapy for BP reduction in these populations. However, it has been suggested that the intrarenal RAS is associated with BP.

**Summary**

In a community sample of African ancestry, which demonstrated typical characteristics of salt sensitivity (inverse relationships between plasma renin concentrations and both BP and an index of salt intake), independent of the systemic RAS (including plasma angiotensinogen concentrations), urinary angiotensinogen/creatinine (an index of urinary angiotensinogen excretion) was associated with both office and 24-hour systolic BP. Hence, despite suppression of the systemic RAS, the intrarenal RAS may play a role in BP control in salt-sensitive groups of African ancestry.
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