PREDICTORS OF PLASMA AND URINARY CATECHOLAMINE LEVELS IN NORMOTENSIVE AND HYPERTENSIVE MEN AND WOMEN

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Abstract

Age, sex, hypertension and dietary sodium are proposed to affect plasma and urinary catecholamines. Yet no prior study has examined the simultaneous effects of these factors within the same study population, so results may have been confounded by factors not determined. We investigate, for the first time, the impact of simultaneously determined predictors of plasma and urinary catecholamines, and the relationship of catecholamines with the diagnosis of hypertension. Hypertensive and normotensive subjects (n=308) were studied off antihypertensives in liberal and low sodium balance. Twenty-four hour urinary catecholamines (norepinephrine and epinephrine) were measured. Plasma catecholamines were measured supine after overnight fast. Repeated measures multivariate linear regression models examined effect of sex, race, age, body mass index, dietary salt (liberal salt vs. low salt), hypertension status, and mean arterial pressure on plasma and urinary catecholamines. Logistic regression determined the relationship of catecholamines with diagnosis of hypertension. Dietary sodium restriction and increasing age predicted increased plasma and urinary norepinephrine, with sodium restriction having greatest effect. Female sex predicted lower urinary and plasma epinephrine. Neither plasma nor urinary catecholamines predicted the diagnosis of hypertension. In summary, specific demographic factors variably impact catecholamines and should be considered when assessing catecholamines in research and clinical settings.

MeSH Keywords

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INTRODUCTION

The sympathetic nervous system plays an important role in blood pressure regulation and response to stress. The level of sympathetic activity is altered by a number of physiologic and pathophysiologic states, including psychosocial and physiologic stress.[1] While elevated plasma and/or urine levels catecholamines are used to diagnose specific conditions such as pheochromocytoma, levels are also used to estimate autonomic nervous system activity and its effect on other disease states, including cardiovascular disease[2–5] and diabetes.[6] Furthermore, elevated plasma catecholamine levels have been shown to predict increased mortality in congestive heart failure[4,5] and cognitive decline and decreased survival in an aging population.[7]

Multiple demographic factors such as age, sex, body mass index (BMI), hypertensive disease and dietary sodium have been shown to potentially affect catecholamine levels in previous studies.[9–19] However, most of these studies consisted of relatively small number of subjects and evaluated effects of individual factors on plasma or urinary catecholamine levels. Therefore findings reported may have been confounded by the factors that were not determined. No prior study has examined the relative effects of all of these factors simultaneously within the same study population. Furthermore, using plasma catecholamine levels as a sole indicator of catecholamine exposure may be problematic due to their short half-life and rapid clearance from circulation, with some studies citing use of 24-hour urinary catecholamines as a preferred measure of integrated catecholamine exposure.[1] The objective of this study was to determine the relative impact of simultaneously determined demographic factors in predicting both plasma and urinary catecholamine levels, in addition to the relationship of catecholamines with the diagnosis of hypertension, in a cohort of hypertensive and normotensive individuals with strict control of environmental factors.

METHODS

Study Population

Subjects (n=308) between the ages of 18 and 65 years were studied by the International Hypertensive Pathotype group at three sites, Brigham and Women's Hospital (Boston, MA), Vanderbilt Medical Center (Nashville, TN) or University of Utah (Salt Lake City, UT).[8] The institutional review committees at each site approved the study protocol, and all subjects provided written, informed consent prior to participating in the study. All subjects completed a screening history and physical and laboratory examination. Subjects were excluded if they had diabetes, coronary artery disease, known or suspected secondary hypertension, stroke, renal insufficiency (serum creatinine>1.5 mg/dL), psychiatric illness, current oral contraceptive use, current tobacco/illicit drug use or alcohol intake greater than 12 oz/week, or any other significant medical illness except obesity. Subjects were also excluded if they demonstrated abnormal electrolytes, thyroid or liver function tests, or electrocardiographic evidence of heart block, ischemia, or prior coronary events at the screening exam. Race was self-defined.

Hypertensive subjects were enrolled if they demonstrated seated diastolic blood pressure of at least 100 mm Hg off antihypertensive medication, DBP at least 90 mm Hg with one or

more medications, or treatment with two or more anti-hypertensive medications. Normotensive subjects were confirmed to have blood pressure less than 140/90 mmHg and no immediate family members with hypertension onset prior to age 60. Antihypertensive medications were discontinued in all subjects at least two weeks before the study.

Study Procedures

Subjects completed two one-week isocaloric dietary phases: a liberal sodium phase (200–250 mEq of sodium per day) and a low-sodium phase (10 mEq per day). Each isocaloric diet contained 100 mEq of potassium per day and was free of caffeine and alcohol. On the final day of each diet, subjects were admitted to the General Clinical Research Center and remained fasting and supine overnight. Subjects were weighed and measured on admission using a standard medical scale (Tanita Corp. of America, Arlington Heights, IL). Body mass index (BMI) was calculated as weight/height (kg/m^2). Twenty-four hour urine collections were used to confirm sodium balance (greater than150 mmol for liberal sodium and less than 30 mmol for low sodium) and for measurement of urinary norepinephrine, epinephrine, and creatinine. All subjects analyzed in this study had complete 24-hour urinary collections that were completed during an overnight stay in the Clinical Research Center. Blood pressure and laboratory assessments, including plasma norepinephrine and epinephrine, were made in the morning after an overnight fast with the subjects supine overnight. Blood was sampled from an intravenous catheter line, with indwelling line placement at least 30 minutes prior to blood sampling. Mean arterial pressure (MAP) was measured and reported as the mean of five consecutive readings using an automated blood pressure monitor (DINAMAP; GE Healthcare, Little Chalfont, UK). Only subjects with complete 24-hour urinary collections, as determined by urinary creatinine, were included in the analysis.

Laboratory Assays

Blood samples were collected on ice in EDTA tubes and centrifuged in a refrigerated centrifuge. Urinary samples were kept refrigerated until completion of 24-hour collection. At that time, urinary samples were aliquoted with the addition of 50 *u*L of 6N HCL to the urine aliquot tube. Plasma and urinary catecholamine levels were measured using extracted radioimmunoassay (IBL America, Minneapolis, MN) and urinary sodium was measured using autoanalyzer techniques. The inter assay variation for plasma norepinephrine and epinephrine was 5.6–10.1% and for urinary norepinephrine and epinephrine was 9.5–13.7%.

Statistical Analysis

Sex, race, age, BMI, dietary salt exposure (high salt vs. low salt), hypertension status, and mean arterial pressure (MAP) were demographic variables of interest. Of these variables, age, BMI and MAP were treated as continuous variables, whereas sex, race, dietary salt exposure, and hypertension status were treated as categorical variables. Due to the small numbers of subjects who self-identified as Asian or Latino, race was categorized into two categories: Black and non-Black. Analysis of variance, followed by Tukey's test for multiple comparisons, was used to assess differences in age, BMI, MAP, and urinary sodium in the categorical variables sex and hypertensive status. Comparisons of plasma catecholamine levels to urinary catecholamine levels were performed individually by

calculation of Pearson's correlation coefficient. Logistic regression was used to determine the ability of plasma or urinary catecholamines to predict presence of hypertensive disease, adjusted for age and BMI. Repeated measures multivariate linear regression models were used to examine the individual effect of age, sex, hypertension status, dietary salt exposure, race, and BMI covariates on plasma and urinary epinephrine and norepinephrine levels. Best-fit lines were obtained using the least-squares method (SAS 9.2, SAS Institute, Cary, NC).

RESULTS

Subject Demographics

Hypertensive subjects were significantly older than their normotensive subjects [$F_{(3,307)}=18.0$, $p<0.0001$] (Table 1). There were no significant age differences between hypertensive men and hypertensive women, or between normotensive men and normotensive women. The hypertensive population did have a significantly higher BMI compared to their normotensive counterparts, [$F_{(3,304)}=23.3$, $p<0.0001$] (Table 1). These differences were consistent within both sexes. There was no significant difference in racial distribution comparing hypertensive subjects with normotensive subjects. However, within the hypertensive subjects, there was an increased proportion of hypertensive women who were Black compared with hypertensive men [$\chi^2=8.4$, $p=0.04$].

In liberal sodium balance, male and female hypertensive subjects demonstrated elevated MAP compared to normotensive subjects [$F_{(3,289)}=114.2$, $p<0.0001$] (Table 1). However, among normotensive subjects, men demonstrated significantly higher MAP than women, $p=0.03$. In low sodium balance, hypertensive subjects also demonstrated significantly higher MAP, compared with normotensive subjects [$F_{(3,288)}=78.8$, $p<0.0001$] while normotensive men continued to have higher MAP than women ($p<0.0001$).

In liberal sodium balance, hypertensive men had significantly higher 24-hour urinary sodium excretion than both hypertensive and normotensive women [$F_{(3,292)}=6.9$, $p=0.0002$], (Table 1). There were no differences in 24-hour urinary sodium excretion between hypertensive and normotensive men, nor were there differences between normotensive men and women. Finally, in low sodium balance, hypertensive men had significantly higher 24-hour urinary sodium excretion than both hypertensive and normotensive women [$F_{(3,291)}=4.2$, $p=0.007$], (Table 1). There were no differences in 24-hour urinary sodium excretion between hypertensive men and hypertensive women, nor were there differences between normotensive men and normotensive women.

Predictors of Hypertension in Study Population

Using logistic regression, the ability of plasma and urinary catecholamines to predict presence of hypertension was tested, adjusted for age, race, BMI and dietary sodium exposure. Neither plasma nor urinary norpepinephrine or epinephrine levels were associated with the diagnosis of hypertension. Similarly, the change in catecholamine levels between liberal sodium diet to low sodium diet was also not associated with the diagnosis of hypertension. Within our study population, only age and BMI were significantly associated

with the diagnosis of hypertension. Of these variables, increasing age resulted in slightly increased odds of diagnosis of hypertension, OR 1.06 (1.03, 1.09, p<0.0001) per year increase in age. Increased BMI had a stronger relationship with diagnosis of hypertension, OR 1.24 (1.15, 1.34, p<0.0001) per unit increase in BMI.

Plasma and Urinary Norepinephrine

In either liberal or low sodium balance, no differences in plasma norepinephrine levels were observed between hypertensive and normotensive populations. In addition, there were no sex differences in plasma norepinephrine levels (Table 3).

In liberal sodium balance, no significant differences in 24-hour urinary norepinephrine levels were observed between hypertensive and normotensive subjects. In addition, there were no sex differences in urinary norepinephrine levels (Table 3). In low sodium balance, however, hypertensive men demonstrated significantly higher urinary norepinephrine levels than normotensive women [F(3,290)=3.4, p=0.002]. No significant differences were observed between hypertensive and normotensive men, or hypertensive and normotensive women.

Predictors of Plasma and Urinary Norepinephrine

Using repeated measures multivariate linear regression, the relative effects of hypertension status, sex, race, age, dietary salt, BMI and MAP on plasma and urinary norepinephrine were assessed. Of these predictors, only age, Black race, and low salt diet significantly predicted plasma norepinephrine levels (Table 2). Controlling for the other variables, as age increases, there is an increase in plasma norepinephrine (β= 2.1, SE=0.8, p=0.005). Black subjects had a significantly higher plasma norepinephrine level (β=50.2, SE 23.0, p=0.03). Low dietary sodium exerted the most significant effect on plasma norepinephrine, with higher plasma norepinephrine levels on the low salt diet (β=64.9, SE=11.5, p<0.0001).

With respect to 24-hour urinary norepinephrine, there were a greater number of significant predictors. Female sex resulted in significantly lower urinary norepinephrine levels (β= −10.7, SE=3.5, p=0.002). In contrast, as BMI increased, urinary norepinephrine increased (β=1.5, SE=0.4, p=0.0009). Similar to its effect on plasma norepinephrine, low dietary sodium also exerted the most significant effect on urinary norepinephrine (β=16.4, SE=2.0, p<0.0001). Age had a weaker but significant effect on urinary norepinephrine (β=0.5, SE=0.2, p=0.005). Race did not significantly predict urinary norepinephrine levels, controlling for other variables. There were no interaction effects of race by sex in the prediction of plasma or urinary norepinephrine.

Plasma and Urinary Epinephrine

In liberal sodium balance, hypertensive men demonstrated significantly higher plasma epinephrine levels than normotensive women [F(3,259)=3.7, p=0.01] (Table 5). However, no significant differences were observed between hypertensive and normotensive men, or hypertensive and normotensive women. In low sodium balance, no differences in plasma epinephrine levels were observed between hypertensive and normotensive populations or men and women.

In liberal sodium balance, hypertensive men demonstrated significantly higher 24-hour urinary epinephrine levels than normotensive women [$F_{(3,293)}=8.3$, $p<0.0001$] (Table 5). However, no significant differences were observed between hypertensive and normotensive men, or hypertensive and normotensive women. In low sodium balance, hypertensive men demonstrated significantly higher urinary epinephrine levels than both hypertensive women and normotensive women [$F_{(3,290)}=8.0$, $p<0.0001$]. In addition, hypertensive men had significantly higher urinary epinephrine levels than hypertensive women in low sodium balance, $p=0.0006$. Similarly, normotensive men demonstrated higher urinary epinephrine levels than normotensive women in low sodium balance, $p=0.045$. There were no interaction effects of race by sex in the prediction of plasma or urinary epinephrine.

Predictors of Plasma and Urinary Epinephrine

In a similar fashion, the relative effects of hypertension status, sex, race, age, dietary salt, BMI and MAP on plasma and urinary epinephrine were assessed. Of these predictors, only female sex and low salt diet significantly predicted plasma epinephrine levels (Table 4). Controlling for the other variables, female sex resulted in decreased in plasma epinephrine ($\beta=-6.5$, SE=2.9, $p=0.02$). In contrast, low dietary sodium resulted in increased plasma epinephrine ($\beta=4.8$, SE=2.4, $p=0.05$). With respect to 24-hour urinary epinephrine, dietary sodium did not significantly affect levels. Only female sex was a significant predictor of urinary epinephrine, resulting in significantly lower levels ($\beta=-4.1$, SE=0.9, $p<0.0001$).

Correlation of Plasma and Urinary Catecholamine Levels

Plasma norepinephrine in liberal sodium balance exhibited a significant correlation with plasma norepinephrine in low sodium balance ($r=0.37$, $p<0.0001$). Similarly, urinary norepinephrine in liberal sodium balance demonstrated a significant correlation with low sodium urinary norepinephrine ($r=0.20$, $p<0.0001$). Correlation of plasma norepinephrine with urinary norepinephrine in low sodium balance was also significant ($r=0.30$, $p<0.0001$). However, the relationship of plasma norepinephrine to urinary norepinephrine in liberal sodium balance was weaker ($r=0.18$, $p=0.06$).

Plasma epinephrine in liberal sodium balance exhibited a significant correlation with plasma epinephrine in low sodium balance ($r=0.30$, $p<0.0001$). However, urinary epinephrine demonstrated the tightest correlation between liberal sodium balance and low sodium balance ($r=0.60$, $p<0.0001$). Correlation of plasma epinephrine with urinary epinephrine in liberal sodium balance was also significant ($r=0.14$, $p=0.02$). However, the relationship of plasma epinephrine to urinary epinephrine in low sodium balance was weaker ($r=0.11$, $p=0.07$).

DISCUSSION

This study investigates for the first time, the simultaneous and relative effects of several postulated predictors of plasma and urinary catecholamine levels in hypertensive and normotensive men and women. This study demonstrates that neither plasma nor urinary catecholamine levels are predictive of the diagnosis of hypertension when controlling for other predictors. A greater number of predictors were associated significantly with both

plasma and urinary norepinephrine, compared with plasma and urinary epinephrine. With respect to plasma and 24-hour urinary norepinephrine, dietary sodium exerts the most significant influence, with sodium restriction resulting in significant increases in both plasma and urinary norepinephrine levels. Age results in mild increases in both plasma and urinary norepinephrine levels. Black race was a significant predictor of plasma norepinephrine, but not 24-hour urinary norepinephrine. Higher BMI was associated with mildly higher urinary norepinephrine. In contrast, female sex was associated with lower 24-hour urinary norepinephrine. Similarly, female sex was associated with significantly lower plasma and urinary epinephrine levels. Sodium restriction was associated with mild decreases in plasma epinephrine levels. However, no other demographic factors were associated with plasma or urinary epinephrine levels.

Plasma and urinary catecholamine levels have been studied for decades in relation to specific disease states and demographic variables. Development of hypertension was reported to be associated with higher plasma norepinephrine levels[9] and higher epinephrine levels,[10] but other studies indicated no differences between hypertensive and normotensive subjects.[11–13] Limitations of these previously published studies include small sample size and age range of subjects,[11–13] lack of control of dietary sodium,[9,10] and measurement of only plasma catecholamine levels.[10–12] The studies that did control for dietary sodium exposure did not demonstrate differences in catecholamine levels between normotensive and hypertensive subjects.[11–13] Our study confirms the prior findings in a larger subject population with greater diversity of age and racial distribution, compared with earlier studies and controlling for other predictors.

Our results indicate that plasma levels of catecholamines do not tightly correlate with urinary levels of catecholamines. As a result, relationships of plasma catecholamines with various outcomes and disease states may not apply to urinary catecholamine levels and vice versa. Few studies have measured both plasma and urinary catecholamine levels in the same population with control of sodium balance. One study reported both plasma and urinary norepinephrine with control of dietary sodium in a small population of young men, but did not report the relationship of plasma and urinary norepinephrine.[14] A more recent study demonstrated weak or no correlation between plasma and urinary catecholamines in a larger sample size, but the urine samples were either spot or overnight urinary collections, not 24-hour urine collections and were standardized for urinary creatinine,[15] a method that can result in a less accurate estimation of catecholamine exposure.[16]

Previously published studies have examined the effect of dietary salt, but not sex, race, age, BMI, on catecholamine levels, with some studies examining the effects of changes in dietary sodium on plasma catecholamine levels[12,14,17–19] and others examining the relationship with urinary catecholamines.[14,20] These studies consistently demonstrate an increase in plasma and urinary catecholamine levels with sodium restriction, versus liberal sodium intake. Similarly, our study demonstrates increased plasma and urinary norepinephrine and plasma epinephrine, with control of other predictors.

Studies that have examined the effect of sex on catecholamine levels have not controlled for dietary sodium exposure.[9,10,21–23] In general, the studies indicate variable association of sex

with levels of catecholamines, with some studies showing lower plasma catecholamine levels in women compared with men,[10,24] other studies showing lower urinary catecholamines in women,[21–23] and one study showing no sex differences.[9] Typically, study subjects were young healthy volunteers.[21,22,24] One reason for conflicting data may be lack of control of dietary salt intake. In the setting of standardized salt intake, our study found that female sex was associated with significantly lower plasma and urinary epinephrine levels and lower urinary norepinephrine levels.

The relationship between catecholamines and age has also been examined in several studies, with some studies reporting that higher catecholamine levels with older age[7,15,25,26] and another study reporting decreased epinephrine levels with increasing age.[27] None of these studied controlled for dietary sodium exposure. In addition, urinary samples were not 24-hour urine collections, but spot or overnight collections that were standardized for urinary creatinine.[15,26] Our study found only a modest effect of age on urinary and plasma norepinephrine, after adjusting for other factors.

A possible weakness of the study includes the use of plasma and urinary catecholamine levels as a surrogate for autonomic system activity. Urinary catecholamine levels are affected by renal metabolism, whereas plasma catecholamines may vary according to exposure and time of day.[15] In physiologic research settings other measures such as muscle sympathetic neuronal activity (MSNA) or norepinephrine spillover are often used to assess autonomic system function.[28] However, in epidemiologic research and clinical practice, plasma and urinary catecholamines are used to assess autonomic activity, and thus the findings of this study are particularly relevant to those settings. Furthermore, sympathetic activity, as measured by MSNA, was shown to be elevated with dietary sodium restriction,[28] which parallels our findings with plasma and urinary norepinephrine in this study.

Our study has several strengths. It is the first study to examine several postulated predictors of catecholamine levels in the same study subjects and in well determined sodium balance. As subjects in this study were both normotensive and hypertensive, the effect of hypertension was examined with control of other factors including dietary sodium, age, BMI, sex, race, and diagnosis of hypertension in the absence of treatment with antihypertensive medications. The age range of the study subjects was broad, allowing for examination of the association of age on catecholamine levels. Furthermore, plasma and urinary catecholamine levels were measured in the same study subjects, with measurement of both norepinephrine and epinephrine. As a result, multiple predictors that have been purported to affect catecholamine levels were examined with respect to their relative impact on catecholamine levels.

Conclusions

Plasma and urinary catecholamine levels are often used as a measure of autonomic nervous system activity and have been associated with various disease states, including diabetes, cardiovascular disease, and also risk for mortality. Although previous studies have examined predictors of catecholamine levels, none have studied the relative effects of multiple predictors of catecholamine levels in the same population. This study demonstrates for the first time, the relative effects of multiple postulated predictors. Of these, restriction of

dietary sodium resulted in the most significant increase in plasma and urinary norepinephrine levels, with smaller effects on plasma epinephrine. Specific demographic factors had varying impact on plasma and urinary norepinephrine and epinephrine. These factors should be considered when assessing catecholamine levels as a measure of autonomic function in research and clinical use.

ACKNOWLEDGMENTS

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Summary Table

What is Known:	• Specific demographic factors, including dietary sodium, age, race, BMI and gender, have varying impact on catecholamine levels.
	• No prior studies have presented relative impact of all demographic factors in both men and women.
What This Study Adds:	• This study demonstrates the simultaneous and relative effects of multiple postulated predictors of catecholamine levels in both normotensive and hypertensive men and women.
	• This study demonstrates, for the first time, that catecholamine levels, both plasma and urinary, do not differ in hypertensive patients, compared with normotensive subjects, when controlling for other variables.
	• This study demonstrates that neither plasma nor urinary catecholamine levels are associated with the diagnosis of hypertension.

Table 1

Subject Demographics

Variable	Men (n=158)		Women (n=151)	
	Hypertensive (n=77)	Normotensive (n=84)	Hypertensive (n=64)	Normotensive (n=91)
Age (years)	48 ± 10^a	38 ± 12^b	49 ± 10^a	41 ± 11^b
BMI (kg/m2)	29 ± 4^a	25 ± 4^b	29 ± 5^a	25 ± 4^b
Race, n (%)				
Non-Black	67 (89)	71 (86)	44 (72)	78 (87)
Black	8 (11)	12 (14)	17 (28)	12 (13)
Liberal Salt Mean MAP (mmHg)	103 ± 11^a	85 ± 8^b	107 ± 12^a	81 ± 10^c
Low Salt Mean MAP (mmHg)	94 ± 11^a	82 ± 7^b	95 ± 12^a	75 ± 9^c
Liberal Salt Urinary Sodium (mmol/24h)	257 ± 87^a	$226 \pm 78^{a,b}$	197 ± 64^b	218 ± 71^b
Low Salt Urinary Sodium (mmol/24h)	16 ± 11^a	12 ± 9^b	$14 \pm 12^{a,b}$	11 ± 10^b

Mean ± SD

Means displayed within the same row that do not share a superscript differ at p<0.05 by Tukey's honestly significant difference comparison.

Table 2

Predictors of Plasma and Urinary Norepinephrine Levels

Variable	Plasma Norepinephrine (n=308 subjects, 503 observations)	24-hour Urinary Norepinephrine (n=308 subjects, 559 observations)
Hypertension	NS	NS
Female Sex	NS	−10.7 (3.5), [−17.5, −3.8]; p=0.002
Race (Black)	50.2 (23.0), [5.0, 95.4]; p=0.03	NS
Age	2.1 (0.8), [0.7, 3.6]; p=0.005	0.5 (0.2), [0.1, 0.8], p=0.005
Low Sodium Diet	64.9 (11.5), [42.3, 87.5]; p<0.0001	16.4 (2.0), [12.4, 20.4]; p<0.0001
BMI	NS	1.5 (0.4), [0.6, 2.3], p=0.0009
MAP	NS	NS

NS, not significant

β coefficient (Standard Error), [Confidence Intervals]

Table 3

Norepinephrine Levels by Gender, Disease Status and Dietary Sodium Intake

Variable	Men		Women	
	Hypertensive	Normotensive	Hypertensive	Normotensive
Liberal Salt Plasma Norepinephrine (pg/mL)	204 ± 143[a] (n=57)	192 ± 159[a] (n=79)	199 ± 129[a] (n=49)	196 ± 167[a] (n=85)
Low Salt Plasma Norepinephrine (pg/mL)	265 ± 166[a] (n=55)	255 ± 142[a] (n=72)	282 ± 139[a] (n=51)	253 ± 164[a] (n=86)
Liberal Salt Urinary Norepinephrine (ug/24h)	68 ± 31[a] (n=71)	69 ± 42[a] (n=82)	59 ± 26[a] (n=60)	58 ± 30[a] (n=83)
Low Salt Urinary Norepinephrine (ug/24h)	88 ± 36[a] (n=72)	81 ± 39[a,b] (n=81)	72 ± 24[a,b] (n=60)	73 ± 31[b] (n=84)

Mean ± SD

Means displayed within the same row that do not share a superscript differ at p<0.05 by Tukey's honestly significant difference comparison.

Table 4

Predictors of Plasma and Urinary Epinephrine Levels

Variable	Plasma Epinephrine (n=308 subjects, 491 observations)	Urinary Epinephrine (n=308 subjects, 559 observations)
Hypertension	NS	NS
Female Sex	−6.5 (2.9) [−12.2, −0.7]; p=0.02	−4.1 (0.9) [−5.8, −2.4]; p<0.0001
Race (Black)	NS	NS
Age	NS	NS
Low Sodium Diet	4.8 (2.4), [0.1, 9.6]; p=0.05	NS
BMI	NS	NS
MAP	NS	NS

NS, not significant

β coefficient (Standard Error), [Confidence Intervals]

Table 5

Epinephrine Levels by Gender, Disease Status and Dietary Sodium Intake

	Men		Women	
Variable	**Hypertensive**	**Normotensive**	**Hypertensive**	**Normotensive**
Liberal Salt Plasma Epinephrine(pg/mL)	37 ± 32^a (n=57)	$36 \pm 29^{a,b}$ (n=75)	$27 \pm 13^{a,b}$ (n=49)	26 ± 16^b (n=81)
Low Salt Plasma Epinephrine(pg/mL)	36 ± 32^a (n=54)	39 ± 27^a (n=69)	33 ± 24^a (n=51)	33 ± 40^a (n=83)
Liberal Salt Urinary Epinephrine(ug/24h)	13 ± 8^a (n=71)	$14 \pm 7^{a,b}$ (n=82)	10 ± 7^b (n=60)	10 ± 6^b (n=83)
Low Salt Urinary Epinephrine(ug/24h)	13 ± 11^a (n=72)	$14 \pm 9^{a,b}$ (n=81)	$9 \pm 5^{b,c}$ (n=60)	10 ± 5^c (n=84)

Mean ± SD

Means displayed within the same row that do not share a superscript differ at p<0.05 by Tukey's honestly significant difference comparison.