have shown that hypertensive subjects with microalbuminuria are at increased cardiovascular risk. However, the criteria for the diagnosis of microalbuminuria are not clear. This study investigated hypertensive non-diabetic subjects with a normal urinary albumin:creatinine ratio (ACR < 3.5 mg/mmol/L) to determine whether BP influenced the level of albuminuria within the normal range.

Demographic data including office BP and urinary ACR values (analysed by immuno-turbidimetric test) from 426 subjects (Mean age 41.2 y, Female 51%, Treated 68.8%, White 82.9%) was analysed. Subjects were stratified according to office systolic BP into 3 discrete groups (A: 130-149 mmHg, B: 150-169 mmHg and C: 170+ mmHg) for comparison. Mann-Whitney and Kruskal-Wallis ANOVA statistical analyses were used.

Female subjects have significantly raised ACR values with similar BP and treatment status (ACR (all subjects): 1.00 (Female) v. 0.835 (Male) p=0.0002; ACR (untreated): 0.86 (F) v. 0.72 (M) p=0.0342). There were no differences between ethnic groups or specific anti-hypertensive therapy. Subsequent analysis was therefore gender-specific. There was significantly greater mean ACR in both male and female subjects at higher levels of BP (Female ACR: A: 0.88; B: 0.88; C: 1.23 p=0.0016. Male ACR: A: 0.64; B: 0.76; C: 1.05 p=0.0004).

Diabetic subjects with microalbuminuria, irrespective of BP, are treated specifically with ACE inhibitors to delay the onset of nephropathy. In non-diabetic hypertensive patients, this issue is currently unresolved. Our study highlights the important observation that the positive correlation of albuminuria to blood pressure continues into the normal range. Although these subjects clearly do not have overt albuminuria, this highlights the difficulty in determining an arbitrary value for microalbuminuria and thus a guide for drug-specific therapy.

Key Words: Albuminuria, Essential Hypertension, Kidney

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D5 DOPAMINE REGULATION OF PHOSPHOLIPASE D AND BLOOD PRESSURE IN MICE
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D1-like receptors inhibit the proliferation and hypertrophy of vascular smooth muscle cells by suppressing phospholipase D (PLD) activity. We hypothesize that the D5 receptor is the D1-like receptor that inhibits PLD activity and serves to regulate blood pressure via this mechanism. Thus, systolic, diastolic, and mean (MAP) blood pressures were higher in D5 receptor-deficient (MAP, mm Hg=141±4, n=70) than in wild type mice (MAP=85±1, n=67, P<0.05). The renal tubular and vascular distribution of PLD was similar in both strains but expression (units) was 2-fold higher (D5-/-=66±2, D5+/+=34±2, n=3, P<0.05) and activity (units) was 70% greater (D5-/-=5.5±0.5, D5+/+=3.2±0.6; n=3, P<0.05) in D5-/- than in D5+/- mice. In CHO cells expressing D5 receptors but not in control cells, the D1/D5 agonist, fenoldopam (FEN) decreased PLD expression (10 μM, 2 hr) (vehicle=40.2±8.1, FEN=12.9±2.9, n=4, P<0.05) and activity (1 μM, 30 min) (vehicle=0.21±0.02, FEN=0.13±0.01; n, P<0.05). In the basal state, D5 F173L, a D5 receptor that cannot stimulate adenylyl cyclase, produced more reactive oxygen species, ROS (units), (131±27, n=3) than the wild type D5 receptor (81±27, n=3, P<0.05). FEN (5 M, 30 min) transiently increased ROS production to a greater extent in D5 F173L (1041±130, n=3) than in wild type D5 receptor (585±78, n=3, P<0.05). We suspect that the hypertension in the D5-/- mice is caused, in part, by increased PLD expression and increased generation of ROS.

Key Words: Phospholipase D, Reactive Oxygen Species, Dopamine Receptor

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CYSTATIN C VERSUS CREATININE IN RENOVASCULAR DISEASE
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Objective: We investigated if cystatin C, a reliable marker of GFR, may serve as a more sensitive discriminant than creatinine in a rule-out strategy in the diagnostic work-up for renovascular disease (RVD).

Design: Cystatin C was measured in 150 hypertensive patients with an intermediate to high index of clinical suspicion of RVD and slightly impaired renal function (creatinine concentration < 177 micromol/L). To define RVD diagnostic accuracy of both cystatin C and creatinine, Receiving operator curves (ROC) curves were calculated. As decision thresholds, values corresponding to 90th and 95th percentiles of the distribution in healthy normotensive population were used.

Results: Cystatin C and creatinine were higher in RVD than in RVD-free patients. ROC curves for the two assays resulted quite similar (AUC 0.73 with 95% C.I. 0.64-0.8 and 0.74 with 95% C.I. 0.66-0.82 for cystatin C and creatinine, respectively). However, considering the values corresponding to 90th or 95th percentiles of normotensive population as decision thresholds (0.90-0.93 mg/L for cystatin C and 92.9-97.2 micromol/L for creatinine), cystatin C showed better sensitivity (87.7-92.3%) and negative predictive value (82.2-87.7%) for RVD diagnosis than did creatinine (sensitivity 70.8-72.3%; negative predictive value 74.3-76.5). Odds ratio against the occurrence of true RVD in case of cystatin C < 0.90 mg/L was 4.26.

Conclusion: Cystatin C is a more sensitive discriminant than creatinine in a rule-out strategy in the diagnostic work-up for renovascular disease. Accordingly, hypertensive patients presenting cystatin C<0.90 mg/L have a low probability of RVD and may reasonably be excluded from any other complex diagnostic investigations.

Key Words: Cystatin C, Renovascular Disease, Renal Function

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LOSS OF RENAL RESERVE IN OBSESE HYPERTENSIVE PATIENTS

To demonstrate the effects of obesity on renal hemodynamics and the role of renal kallikrein (kKal) and nitric oxide (NO) on renal response to oral protein load (renal reserve, RR), we studied 14 obese (BMI: 32.9 ± 1.1, age: 50.5 ± 0.9 y, SBP: 152.8 ± 2.4mmHg, DBP 96.2 ± 2.2mmHg, 5 males and 9 females) and 9 non obese hypertensive patients (BMI=22.9 ± 1.1, age 50.6 ± 2.7 y, SBP=151.2 ± 2.8 mmHg, DBP: 97.9 ± 2.1mmHg, 4 males and 5 females). Hemodynamic and metabolic evaluations were conducted at basal conditions and after protein challenge moment (1g/kg of weight). Glomerular filtration rate (GFR) was estimated by clearance of inulin, and renal plasma flow (RPF) was