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A putative role for the G protein-coupled estrogen receptor-1, GPER-1, in the renoprotective effects of estrogen

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Estrogen promotes renoprotective effects that are linked to the G-protein-coupled estrogen receptor-1 (GPER-1). Our studies have shown that GPER-1 immunoreactivity is primarily localized in distal convoluted tubules and the Loop of Henle (stained with Tamm-Horsfall Protein-1). Lower GPER-1 expression is observed in proximal convoluted tubules marked with megalin, and GPER-1 is not readily detected in collecting ducts. Plasma membrane fractions prepared from whole kidney tissue or HEK293 cells expressing recombinant human GPER-1 (HEK-GPER-1) display high-affinity, specific [3H]-17β-estradiol ([3H]-E2) binding, but no specific [3H]-aldosterone binding. In contrast, cytosolic preparations exhibit specific binding to [3H]-aldosterone but not to [3H]-E2, consistent with the subcellular distribution of GPER-1 and mineralocorticoid receptor (MR) in these preparations. Aldosterone and MR antagonists, spironolactone and eplerenone, failed to compete for specific [3H]-E2 binding to membranes of HEK-GPER-1 cells. Furthermore, aldosterone did not increase [35S]-GTP-χS binding to membranes of HEK-GPER-1 cells, indicating that it is not involved in G-protein signaling mediated through GPER-1. During the follicular phases of the estrus cycle, GPER-1 is upregulated on renal cortical epithelia and localized to the basolateral surface during proestrus and redistributed intracellularly during estrus. GPER-1 is down-modulated during the luteal phases of the estrus cycle with significantly less receptor on the surface of renal epithelia, and as measured by gel electrophoretic analysis. Our results demonstrate that GPER-1 is associated with specific estrogen binding and not aldosterone binding and that GPER-1 expression is modulated during the estrus cycle which may suggest a physiological role for GPER-1 in the kidney during reproduction.

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Screening for occult renal disease (SCORED) is a useful tool to identify individuals at high-risk for chronic kidney disease

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Introduction: Screening for chronic kidney disease (CKD) has been advocated with increasing frequency. Population-based studies relating to the prevalence of CKD in the community are limited. We prospectively studied whether stratification by SCORED values could be useful in identifying subjects who are at high-risk for CKD in a general population-based sample.

Methods: The frequency of individuals at high-risk for CKD was determined using a cross-sectional study of 873 adult households in Palmas, Brazil, that were randomly selected using a stratified, cluster method. Age, gender, and race of the study sample were similar to the population of Palmas.

Results: An estimated GFR <60 ml/min/1.73 m2 was present in 46 (5.3%) of the participants studied, and the risk of CKD was greater in women than in men, and increased with age from 2.7% in the 18-44 age group to 19.0% in those ≥65 years. The frequencies of CKD Stage 3, 4 and 5 were 4.8%, 0.5%, and 0%, respectively. The SCORED values included 224 (25.7%) patients with high SCORED values (≥4), and 649 (74.3%) subjects with low SCORED values. The subjects with higher SCORED values were at a significantly higher risk for CKD compared with those who had lower SCORED values (12.9% vs. 2.6%, $\chi 2=35.58$; $p<0.001$). Sensitivity, specificity and negative predictive value for predicting CKD by the SCORED model was 63%, 76%, and 76%, respectively.

Conclusion: High SCORED values were associated with a higher risk for CKD in a general population-based sampling. This simple screening tool was useful in identifying individuals at high-risk for CKD.

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