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INSULIN RESISTANCE IN SUBJECTS WITH IMPAIRED FASTING GLUCOSE AND/OR IMPAIRED GLUCOSE TOLERANCE IS SIGNIFICANTLY ASSOCIATED WITH INTRAGLOMERULAR HYDROSTATIC PRESSURE AND ALBUMINURIA

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INTRODUCTION: Obese and type 2 diabetes patients are well known to exhibit insulin resistance. The development and progression of diabetic nephropathy are associated with glomerular hypertension and hyperfiltration. Glomerular hyperfiltration in diabetic patients contributes to the onset of nephropathy; albuminuria, However, little is known about the relationships between insulin resistance, intrarenal hemodynamics, and urinary albumin excretion (UAE) in humans

with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT). The aim of the present study was to examine intrarenal hemodynamic abnormalities, insulin resistance, and UAE, in subjects with IFG and/or IGT. We hypothesized that intrarenal hemodynamic abnormalities would be associated with insulin resistance.

METHODS: Fifty four kidney donor candidates were admitted and kept under 6g NaCl and standard meals. All subject underwent 75 g oral glucose tolerance under fasting condition in the morning, and insulin sensitivity index (ISI) was evaluated by the Matsuda Index (Matzuda and DeFronzo, Diabetes Care 1999). In another morning under overnight fast, simultaneous measurements of plasma clearance of para-aminohippurate (CPAH), and inulin (Cin) were performed, and intrarenal hemodynamic parameters, such as efferent arteriolar resistance (R-e) and glomerular hydrostatic pressure (Pglo), were calculated by Gomez's formulae (Guidi. Am J Hypertens 2001).

RESULTS: Of the 54 subjects, 33 exhibited IFG and/or IGT, and 31 exhibited normal glucose tolerance (NGT). All subjects showed normal ranges of UAE less (than 30 mg/day). Filtration fraction (Cin/CPAH), Pglo, and UAE were significantly higher in the IFG and/or IGT subjects with obesity ($p=0.016$, $p=0.015$, and 0.0001, respectively). R-e in the IFC and/or IGT subjects with obesity was tended to be higher than in the other groups ($p = 0.066$). ISI in subjects with obesity was significantly lower than in those without obesity ($p < 0.0001$). Log ISI correlated significantly and negatively with Pglo ($r= - 0.351$, $p=0.009$) in all subjects. In multiple regression analyses among all subjects, log ISI was associated significantly and independently with Pglo ($\beta=-0.316$, $p=0.015$), after adjustment for age, gender, and systolic blood pressure. Further, BMI ($\beta=0.517$, $p=0.0004$), Pglo ($\beta=0.420$, $p=0.004$) and log ISI ($\beta= -0.366$, $p=0.008$) were each associated significantly and independently with UAE, after the adjustment.

CONCLUSIONS: In the present study, by measuring Cin and CPAH, we showed that increased insulin resistance (decreased ISI) is associated significantly with increased Pglo and urinary albumin excretion, even at levels currently considered to be within the normal range, in human subjects with IFG and/or IGT. These hemodynamic burdens may lead to glomerular injury in IFG and/or IGT subjects. We also suggest that the clinically significant levels of microalbuminuria (>30mg/day), as currently defined, could be redefined based upon several human studies, including the present study.