Adipose Insulin Resistance Relates to Perturbed Renal Hemodynamics in Obese Youth with and without Type 2 Diabetes.

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Objectives: Our objective was to compare renal hemodynamic function between obese youth with and without type 2 diabetes (T2D) and relate these measures to adipose insulin resistance (IR).

Methods: We assessed insulin sensitivity and kidney function in obese youth with (n=31, 15.8 $\pm$ 1.8 years, BMI 35.6 $\pm$ 6.6 kg/m^2), and without (n=20, 15.3 $\pm$ 2.1 years, BMI 38.2 $\pm$ 7.4 kg/m^2) T2D. A hyperglycemic clamp was performed with 20% dextrose to maintain mild hyperglycemia for 240 minutes. Free fatty acids (FFA) were measured at baseline and every 10 minutes during the steady state. FFA suppression (baseline FFA subtracted from steady state FFA) was used to estimate adipose IR. Iohexol and *p*-aminohippurate clearances were used to measure GFR and renal plasma flow, respectively. Renal hemodynamic parameters were calculated using Gomez equations.

Results: FFA suppression was attenuated in youth with T2D compared to obese controls (55.6% vs. 92.1%, $p<0.0001$). Impaired FFA suppression was associated with higher intraglomerular pressure (r= -0.49, $p=0.005$), higher efferent arteriolar resistance, (r= -0.53, p=0.002) and higher renal vascular resistance (r= -0.59, p=0.0005).

Conclusion: Youth with T2D had impaired FFA suppression compared to obese controls, indicating adipose IR. Impaired FFA suppression was associated with perturbed renal hemodynamics, indicating a potential role for adipose IR in the development of early diabetic kidney disease.