

Adipose Insulin Resistance Relates to Perturbed Renal Hemodynamics in Obese Youth with and without Type 2 Diabetes. C Platnick (MD, SOM), G Shutte, P Prasad, LP Li, L Pyle, C Severn, RG Nelson, D van Raalte, K Nadeau,* P Bjornstad,* Department of Pediatrics, Section of Endocrinology, University of Colorado, Denver, CO.

Objectives: There is a need to better understand the pathophysiology of early diabetic kidney disease (DKD) in youth with type 2 diabetes (T2D). The objective of this study was to compare intrarenal hemodynamic function between obese youth with and without 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 ± 1.8 years, BMI 35.6 ± 6.6 kg/m², HbA1c 6.9 ± 1.6 , 58% female), and without (n=20, 15.3 ± 2.1 years, BMI 38.2 ± 7.4 kg/m², HbA1c 5.45 ± 0.3 , 30% female) T2D. A hyperglycemic clamp was performed with 20% dextrose to maintain mild hyperglycemia (~190-200 mg/dl) for 240 minutes. Free fatty acid (FFA) labs were collected at baseline, and every 10 minutes during the steady state (190-240 minutes). FFA suppression was calculated as baseline FFA subtracted from steady state FFA and used to estimate adipose IR. Iohexol and *p*-aminohippurate clearances were used to measure glomerular filtration rate and renal plasma flow, respectively. Gomez equations were used to calculate parameters of intrarenal hemodynamic function. Statistical comparison was done using the nonparametric Mann Whitney test, and correlations were determined using nonparametric Spearman's rho.

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 (Spearman $r = -0.49$, $p = 0.005$), higher efferent arteriolar resistance, (Spearman $r = -0.53$, $p = 0.002$) and higher renal vascular resistance (Spearman $r = -0.59$, $p = 0.0005$).

Conclusions: Youth with T2D exhibited impaired FFA suppression compared to obese control participants, indicating adipose IR. Impaired FFA suppression was associated with perturbed renal hemodynamic parameters, indicating a potential role for adipose tissue IR in the development of early DKD.

Figure 1.

