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.

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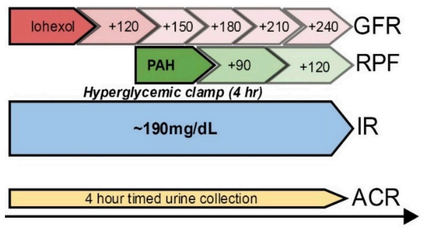
Objectives

- There is a need to better understand the pathophysiology of early intraglomerular hemodynamic dysfunction in youth with type 2 diabetes (T2D).
- The objective of this study was to compare adipose insulin sensitivity between obese youth with and without T2D and relate this measure to intraglomerular function.

Methods

- We assessed insulin sensitivity and intraglomerular hemodynamic function in obese youth with and without T2D.



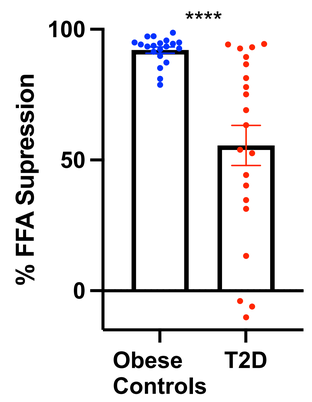
- Gomez equations were used to calculate parameters of intraglomerular hemodynamic function.
- Statistical comparison was done using the nonparametric Mann Whitney test, and correlations were determined using nonparametric Spearman's rho.

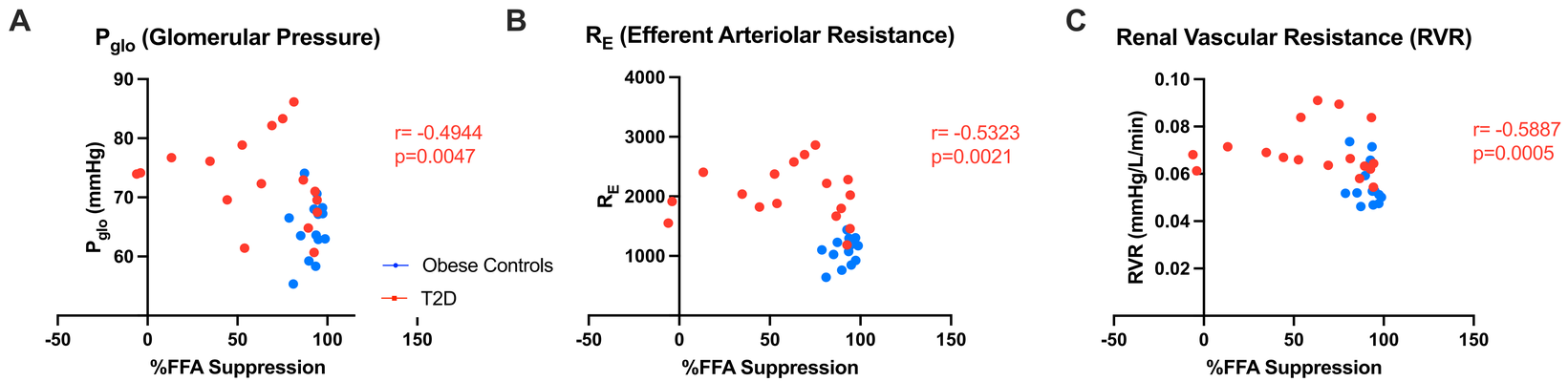
Results

- Free fatty acid (FFA) suppression was lower in youth with T2D compared to obese controls (55.6% vs. 92.1%, $p<0.0001$) (right), indicating ***adipose insulin resistance (IR)***.

- Impaired FFA suppression was associated with higher intraglomerular pressure, higher efferent arteriolar resistance, and higher renal vascular resistance (below).

	Obese Controls (n=20)	T2D (n=31)
A1c (%)	5.3 ±0.1	5.8 ±0.8
BMI (kg/m²)	38.2 ±7.4	35.6 ±6.6
HbA1c (%)	5.5 ±0.3	6.9 ±1.6
Female	30%	58%





Conclusion: Impaired FFA suppression was associated with perturbed renal hemodynamic parameters, indicating a potential role for adipose tissue IR in the development of early DKD.
These findings may be explained by the fact that FFAs are a less efficient energy substrate for the kidneys compared to glucose -- with less ATP produced per oxygen consumed -- driving increased renal oxygen consumption and ultimately leading to oxidative damage and endothelial dysfunction.