

Supplemental Table 1 Intraglomerular hemodynamic function, MRI, DXA, and hyperglycemic clamp measures by albuminuria in youth with type 2 diabetes

	Normoalbuminuria (N=35)	Elevated albuminuria (N=15)	p value
<i>Anthropometrics</i>			
BMI (kg/m ²)	34.9 ± 7.5	40.4 ± 5.6	0.016
Weight (kg)	99.8 ± 24.5	114.4 ± 22.1	0.059
Height (cm)	167.8 ± 9.0	168.8 ± 7.7	0.691
<i>Intraglomerular hemodynamic function</i>			
GFR (mL/min)	207 ± 58	213 ± 77	0.755
GFR (mL/min/1.73m ²)	166 ± 39	155 ± 48	0.440
RPF (mL/min)	833 ± 180	921 ± 117	0.142
RPF (mL/min/1.73m ²)	663 ± 115	661 ± 74	0.950
FF (%)	25 ± 7	22 ± 5	0.163
P _{GLO} (mmHg)	79 ± 11	79 ± 11	0.938
R _A (dyne·s·cm ⁻⁵)	866 ± 379	859 ± 780	0.972
R _E (dyne·s·cm ⁻⁵)	2301 [1900, 2464]	1894 [1596, 2222]	0.097
RVR (mm Hg/L/min·1000)	0.07 ± 0.01	0.06 ± 0.01	0.043
<i>Multiparametric kidney MRI</i>			
Left cortex 3D ASL (mL/min/100g)	212.4 ± 56.0	203.3 ± 34.5	0.667
Right cortex 3D ASL (mL/min/100g)	223.5 ± 45.3	224.8 ± 50.6	0.943
Average cortex 3D ASL (mL/min/100g)	218.6 ± 49.3	215.1 ± 38.6	0.841
Left cortex R2* (s ⁻¹)	18.3 ± 1.3	17.5 ± 0.9	0.060
Right cortex R2* (s ⁻¹)	17.5 ± 1.6	18.6 ± 3.4	0.147
Average cortex R2* (s ⁻¹)	17.9 ± 1.2	18.4 ± 2.8	0.413
Left medulla R2* (s ⁻¹)	25.0 ± 3.1	23.8 ± 3.0	0.315
Right medulla R2* (s ⁻¹)	23.9 ± 2.6	24.8 ± 3.9	0.391
Average medulla R2* (s ⁻¹)	24.4 ± 2.7	24.7 ± 3.9	0.707
Left FSOC medulla (%)	5.4 ± 3.2	4.8 ± 4.1	0.641
Right FSOC medulla (%)	5.2 ± 2.3	4.8 ± 3.0	0.645
Average FSOC medulla (%)	5.3 ± 2.6	4.7 ± 3.3	0.600
<i>DXA</i>			
Lean mass (kg)	54.4 ± 10.4	59.6 ± 12.3	0.142
Fat mass (kg)	39.5 ± 14.6	52.7 ± 11.3	0.004
Body fat percentage (%)	41.5 ± 7.0	46.7 ± 4.6	0.013
Trunk mass (kg)	46.0 ± 12.8	56.9 ± 10.8	0.007
<i>Hyperglycemic clamp measures</i>			
Fasting FFA	693.6 ± 197.7	772.5 ± 239.0	0.312
FFA suppression (%)	72.1 [45.2, 91.6]	38.7 [24.5, 71.0]	0.066
Fasting insulin (pM)	14.5 [8.5, 21.0]	22.0 [15.4, 31.3]	0.045
Steady state insulin (pM)	205.5 [85.5, 379.5]	282.8 [76.5, 421.1]	0.780
Steady state C-peptide (nM)	7.8 ± 4.2	9.0 ± 5.6	0.438
Raw M-value (mg/kg lean/min)	4.0 ± 2.9	2.6 ± 1.9	0.110
M/I (mg/kg lean/min) / (pM)	0.015 [0.009, 0.029]	0.009 [0.002, 0.013]	0.016
DI (x10 ³ mg/kg lean/min)	0.8 [0.1, 2.0]	0.07 [0.0, 0.7]	0.031
AIRg (pM)	40.0 [0.0, 118.2]	15.6 [0.0, 72.0]	0.259
ACPRg (nM)	0.7 [0.3, 1.5]	0.5 [0.0, 0.8]	0.336

Continuous variables are shown as means ± standard deviations or median and 25th, 75th percentiles in square brackets. Categorical variables are shown as counts and percentages in parentheses.

Abbreviations: GFR, glomerular filtration rate; RPF, effective renal plasma flow; FF, filtration fraction; P_{GLO}, glomerular pressure; R_A, afferent arteriolar resistance; R_E, efferent arteriolar resistance; RVR, renal vascular resistance; MRI, magnetic resonance imaging; TKV, total kidney volume, 3D ASL, 3-dimensional arterial spin labeling; ADC, afferent diffusion coefficient; FSOC, furosemide-induced suppression of oxygen consumption; DXA, dual-energy X-ray absorptiometry; FFA, free fatty acid; M/I, insulin sensitivity index (M-value/mean insulin concentration); DI, disposition index; AIRg, acute insulin response to glucose; ACPRg, acute C-peptide response to glucose.

Supplemental Table 2 Intraglomerular hemodynamic function, MRI, DXA, and hyperglycemic clamp measures by hyperfiltration (by mGFR) in youth with type 2 diabetes

	No hyperfiltration (N=22)	Hyperfiltration (N=26)	p value
<i>Anthropometrics</i>			
BMI (kg/m ²)	35.6 ± 6.8	37.1 ± 8.0	0.493
Weight (kg)	100.8 ± 22.0	106.3 ± 27.0	0.446
Height (cm)	168.0 ± 8.1	168.7 ± 8.2	0.775
<i>Intraglomerular hemodynamic function</i>			
GFR (mL/min)	163 ± 33	250 ± 55	< 0.001
GFR (mL/min/1.73m ²)	128 ± 21	193 ± 30	< 0.001
RPF (mL/min)	808 ± 129	904 ± 190	0.068
RPF (mL/min/1.73m ²)	636 ± 92	689 ± 112	0.105
FF (%)	21 ± 5	28 ± 6	< 0.001
P _{GLO} (mmHg)	72 ± 8	86 ± 9	< 0.001
R _A (dyne·s·cm ⁻⁵)	1032 ± 535	626 ± 344	0.018
R _E (dyne·s·cm ⁻⁵)	1731 [1503, 2040]	2391 [2276, 2483]	< 0.001
RVR (mm Hg/L/min·1000)	0.07 ± 0.01	0.06 ± 0.02	0.791
<i>Multiparametric kidney MRI</i>			
Average cortex 3D ASL (mL/min/100g)	218.6 ± 57.2	215.2 ± 35.2	0.832
Average cortex R2* (s ⁻¹)	18.3 ± 2.1	17.9 ± 1.3	0.535
Average medulla R2* (s ⁻¹)	25.6 ± 3.0	23.5 ± 2.9	0.023
Average FSOC medulla (%)	5.7 ± 2.8	4.6 ± 2.8	0.218
<i>DXA</i>			
Lean mass (kg)	55.4 ± 8.2	57.0 ± 13.5	0.639
Fat mass (kg)	40.7 ± 15.2	46.1 ± 14.6	0.229
Body fat percentage (%)	42.0 ± 7.7	43.8 ± 5.6	0.354
Trunk mass (kg)	46.9 ± 13.1	51.7 ± 13.2	0.234
<i>Hyperglycemic clamp measures</i>			
Fasting FFA (μM)	698.9 ± 218.1	728.2 ± 205.1	0.673
FFA suppression (%)	66.2 [44.6, 91.8]	67.6 [32.8, 79.9]	0.438
Fasting insulin (pM)	17.8 [7.6, 22.2]	16.5 [9.0, 29.0]	0.685
Steady state insulin (pM)	190.5 [82.1, 419.2]	235.5 [82.5, 387.0]	0.717
Steady state C-peptide (nM)	8.6 ± 5.1	7.7 ± 4.1	0.520
Raw M-value (mg/kg lean/min)	4.2 ± 3.1	3.1 ± 2.2	0.168
M/I (mg/kg lean/min) / (pM)	0.011 [0.005, 0.021]	0.012 [0.007, 0.022]	0.783
DI (x10 ³ mg/kg lean/min)	0.8 [0.0, 1.9]	0.3 [0.0, 1.4]	0.599
AI _{Rg} (pM)	30.0 [0.0, 97.2]	33.6 [0.0, 118.2]	0.796
ACPR _g (nM)	0.6 [0.3, 1.2]	0.6 [0.2, 1.5]	1.000

Two participants were excluded from this table due to missing mGFR data.

Continuous variables are shown as means ± standard deviations or median and 25th, 75th percentiles in square brackets. Categorical variables are shown as counts and percentages in parentheses.

Abbreviations: GFR, glomerular filtration rate; RPF, effective renal plasma flow; FF, filtration fraction; P_{GLO}, glomerular pressure; R_A, afferent arteriolar resistance; R_E, efferent arteriolar resistance; RVR, renal vascular resistance; MRI, magnetic resonance imaging; TKV, total kidney volume, 3D ASL, 3-dimensional arterial spin labeling; ADC, afferent diffusion coefficient; FSOC, furosemide-induced suppression of oxygen consumption; DXA, dual-energy X-ray absorptiometry; FFA, free fatty acid; M/I, insulin sensitivity index (M-value/mean insulin concentration); DI, disposition index; AI_{Rg}, acute insulin response to glucose; ACPR_g, acute C-peptide response to glucose.

Supplemental Table 3 MRI measures by group

	Controls in Normal Weight Category (N=20)	Controls with Obesity (N=21)	Youth with Type 2 Diabetes (N=50)	Pairwise difference [†]	p value
<i>Multiparametric kidney MRI</i>					
Left cortex 3D ASL (mL/min/100g)	192.1 ± 52.4	190.4 ± 40.5	210.3 ± 51.6	-	0.278
Right cortex 3D ASL (mL/min/100g)	201.7 ± 56.2	199.6 ± 47.3	223.9 ± 46.1	-	0.127
Average cortex 3D ASL (mL/min/100g)	196.9 ± 53.4	195.6 ± 45.7	217.7 ± 46.2	-	0.158
Left cortex R2* (s ⁻¹)	22.2 ± 2.6	19.1 ± 2.0	18.1 ± 1.3	NT*, NO*	< 0.001
Right cortex R2* (s ⁻¹)	20.4 ± 2.4	18.8 ± 2.6	17.8 ± 2.3	NT*	< 0.001
Average cortex R2* (s ⁻¹)	21.2 ± 2.3	18.9 ± 2.2	18.0 ± 1.8	NT*, NO	< 0.001
Left medulla R2* (s ⁻¹)	29.3 ± 3.4	25.0 ± 3.2	24.7 ± 3.1	NT*, NO*	< 0.001
Right medulla R2* (s ⁻¹)	26.6 ± 3.1	24.2 ± 2.9	24.2 ± 3.0	NT, NO	0.008
Average medulla R2* (s ⁻¹)	27.8 ± 3.0	24.6 ± 2.8	24.5 ± 3.1	NT*, NO	< 0.001
Left FSOC medulla (%)	6.3 ± 2.5	3.4 ± 2.3	5.3 ± 3.4	NO	0.018
Right FSOC medulla (%)	5.3 ± 2.2	3.4 ± 2.1	5.1 ± 2.5	OT, NO	0.024
Average FSOC medulla (%)	5.7 ± 1.9	3.4 ± 1.9	5.1 ± 2.8	NO	0.014

Continuous variables are shown as means ± standard deviations or median and 25th, 75th percentiles in square brackets. Categorical variables are shown as counts and percentages in parentheses.

Abbreviations: 3D ASL, 3-dimensional arterial spin labeling; FSOC, furosemide-induced suppression of oxygen consumption.

[†]Pair abbreviations are shown if pairwise test is significant at p<0.05. Pairwise abbreviations: OT, controls with obesity versus youth with type 2 diabetes; NT, controls in normal weight category versus youth with type 2 diabetes; NO, controls in normal weight category versus controls with obesity. *p < 0.001.

Supplemental Table 4 Correlation coefficients with all participants combined

	GFR	RPF	P _{GLO}	RVR	Average cortex R2*	Average medulla R2*	Average FSOC medulla
Lean mass (%)	-0.437 <i><0.001</i>	-0.484 <i><0.001</i>	-0.453 <i><0.001</i>	0.331 <i>0.006</i>	0.469 <i><0.001</i>	0.496 <i><0.001</i>	0.346 <i>0.002</i>
Fat mass (kg)	0.623 <i><0.001</i>	0.730 <i><0.001</i>	0.519 <i><0.001</i>	-0.614 <i><0.001</i>	-0.441 <i><0.001</i>	-0.480 <i><0.001</i>	-0.508 <i><0.001</i>
Body fat (%)	0.434 <i><0.001</i>	0.490 <i><0.001</i>	0.414 <i><0.001</i>	-0.352 <i>0.003</i>	-0.463 <i><0.001</i>	-0.499 <i><0.001</i>	-0.373 <i><0.001</i>
Trunk mass (kg)	0.695 <i><0.001</i>	0.738 <i><0.001</i>	0.611 <i><0.001</i>	-0.625 <i><0.001</i>	-0.424 <i><0.001</i>	-0.442 <i><0.001</i>	-0.539 <i><0.001</i>
Urine Albumin-Creatinine Ratio	-0.016 <i>0.885</i>	0.131 <i>0.273</i>	0.260 <i>0.029</i>	-0.048 <i>0.694</i>	-0.181 <i>0.095</i>	-0.145 <i>0.185</i>	-0.091 <i>0.418</i>
HbA1C (%)	0.260 <i>0.015</i>	0.387 <i><0.001</i>	0.616 <i><0.001</i>	-0.293 <i>0.014</i>	-0.438 <i><0.001</i>	-0.378 <i><0.001</i>	0.001 <i>0.994</i>
Average cortex R2*	-0.420 <i><0.001</i>	-0.267 <i>0.027</i>	-0.450 <i><0.001</i>	0.275 <i>0.025</i>	1.000 <i><0.001</i>	0.684 <i><0.001</i>	0.203 <i>0.069</i>
Average medulla R2*	-0.406 <i><0.001</i>	-0.252 <i>0.038</i>	-0.366 <i>0.002</i>	0.228 <i>0.065</i>	0.684 <i><0.001</i>	1.000 <i><0.001</i>	0.623 <i><0.001</i>
Average FSOC medulla	-0.33 <i>0.003</i>	-0.289 <i>0.021</i>	-0.191 <i>0.134</i>	0.213 <i>0.097</i>	0.203 <i>0.069</i>	0.623 <i><0.001</i>	1.000 <i><0.001</i>

Abbreviations: GFR, glomerular filtration rate; RPF, effective renal plasma flow; P_{GLO}, glomerular pressure; RVR, renal vascular resistance; FSOC, furosemide-induced suppression of oxygen consumption; HbA1c: glycated hemoglobin.

Supplemental Table 5 Correlation coefficients limited to youth with type 2 diabetes and controls with obesity

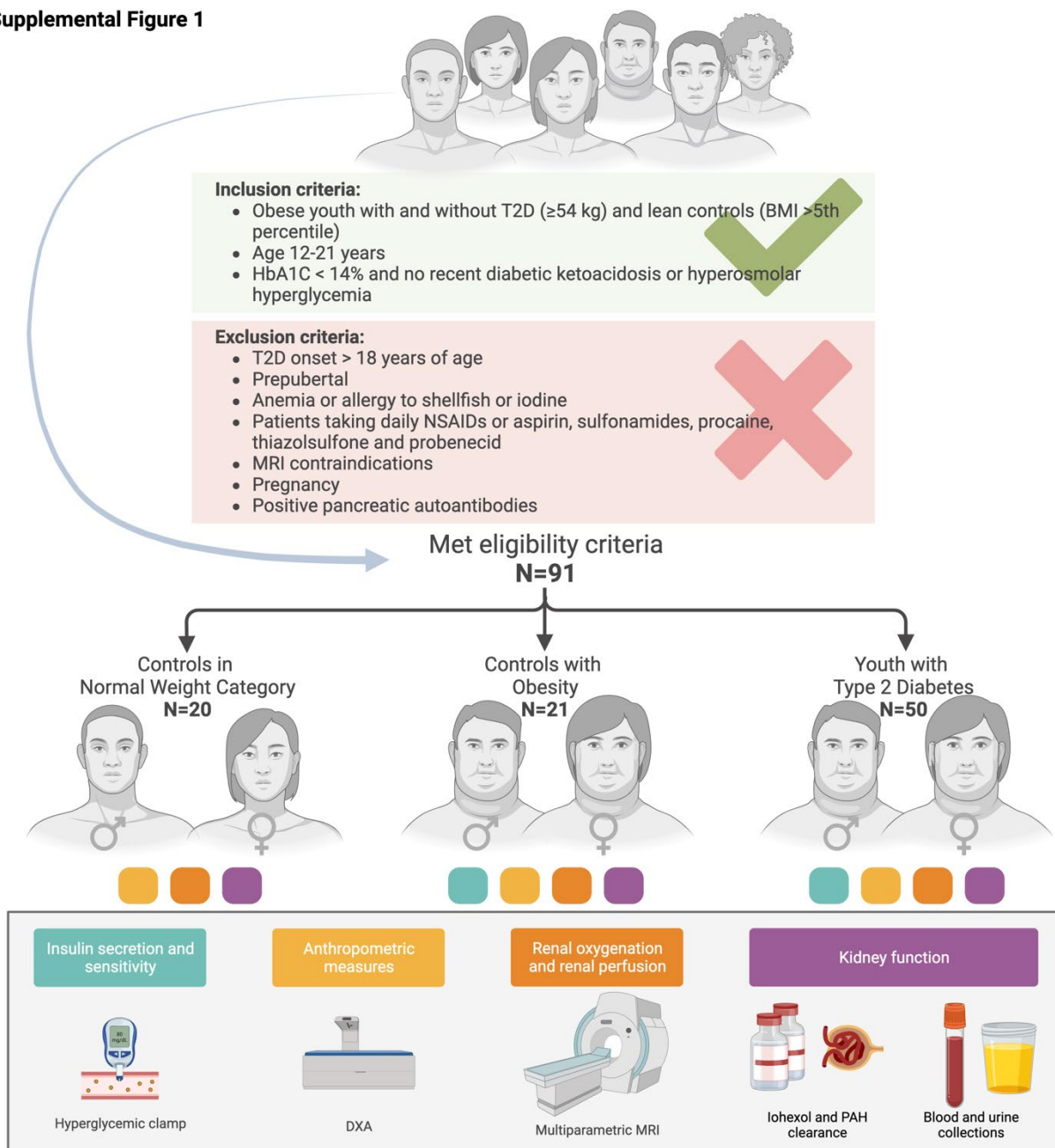
	GFR	RPF	P _{GLO}	RVR	Average cortex R2*	Average medulla R2*	Average FSOC medulla
Lean mass (%)	-0.184 <i>0.139</i>	-0.204 <i>0.139</i>	-0.101 <i>0.465</i>	-0.035 <i>0.808</i>	0.118 <i>0.360</i>	0.337 <i>0.008</i>	0.351 <i>0.007</i>
Fat mass (kg)	0.447 <i><0.001</i>	0.588 <i><0.001</i>	0.208 <i>0.131</i>	-0.456 <i><0.001</i>	-0.117 <i>0.367</i>	-0.307 <i>0.016</i>	-0.531 <i><0.001</i>
Body fat (%)	0.191 <i>0.124</i>	0.239 <i>0.082</i>	0.057 <i>0.682</i>	-0.037 <i>0.797</i>	-0.125 <i>0.334</i>	-0.349 <i>0.006</i>	-0.392 <i>0.002</i>
Trunk mass (kg)	0.548 <i><0.001</i>	0.588 <i><0.001</i>	0.345 <i>0.011</i>	-0.458 <i><0.001</i>	-0.088 <i>0.498</i>	-0.251 <i>0.051</i>	-0.552 <i><0.001</i>
Fasting FFA	-0.138 <i>0.300</i>	0.013 <i>0.927</i>	0.042 <i>0.775</i>	0.067 <i>0.652</i>	0.161 <i>0.240</i>	0.096 <i>0.488</i>	0.057 <i>0.688</i>
FFA Suppression	0.211 <i>0.112</i>	0.156 <i>0.285</i>	-0.331 <i>0.022</i>	-0.263 <i>0.071</i>	0.016 <i>0.907</i>	-0.015 <i>0.913</i>	-0.282 <i>0.043</i>
Fasting Insulin	0.188 <i>0.129</i>	0.275 <i>0.042</i>	0.270 <i>0.048</i>	-0.137 <i>0.327</i>	-0.348 <i>0.005</i>	-0.400 <i>0.001</i>	-0.443 <i><0.001</i>
Steady State Insulin	0.168 <i>0.175</i>	0.261 <i>0.054</i>	-0.220 <i>0.109</i>	-0.302 <i>0.028</i>	-0.116 <i>0.360</i>	-0.118 <i>0.353</i>	-0.455 <i><0.001</i>
Steady State C-Peptide	0.122 <i>0.345</i>	0.292 <i>0.040</i>	-0.217 <i>0.134</i>	-0.439 <i>0.002</i>	-0.109 <i>0.397</i>	-0.084 <i>0.518</i>	-0.407 <i>0.001</i>
Raw M-value	0.050 <i>0.689</i>	-0.021 <i>0.881</i>	-0.378 <i>0.005</i>	-0.189 <i>0.176</i>	0.042 <i>0.741</i>	0.103 <i>0.423</i>	-0.082 <i>0.534</i>
M/I	-0.133 <i>0.286</i>	-0.400 <i>0.003</i>	0.067 <i>0.632</i>	0.287 <i>0.039</i>	0.250 <i>0.048</i>	0.253 <i>0.046</i>	0.414 <i><0.001</i>
DI	0.023 <i>0.857</i>	-0.080 <i>0.569</i>	-0.343 <i>0.013</i>	-0.063 <i>0.662</i>	0.015 <i>0.909</i>	0.087 <i>0.501</i>	-0.219 <i>0.095</i>
AI _{Rg}	0.139 <i>0.265</i>	0.066 <i>0.638</i>	-0.245 <i>0.077</i>	-0.174 <i>0.217</i>	-0.089 <i>0.489</i>	-0.049 <i>0.702</i>	-0.401 <i>0.001</i>
ACPR _g	0.167 <i>0.198</i>	0.153 <i>0.295</i>	-0.255 <i>0.080</i>	-0.327 <i>0.025</i>	-0.042 <i>0.749</i>	-0.003 <i>0.983</i>	-0.376 <i>0.003</i>
HbA1C (%)	-0.033 <i>0.787</i>	0.013 <i>0.925</i>	0.421 <i>0.001</i>	0.097 <i>0.484</i>	-0.165 <i>0.185</i>	-0.198 <i>0.114</i>	0.162 <i>0.209</i>
Average cortex R2*	-0.185 <i>0.143</i>	0.001 <i>0.992</i>	-0.272 <i>0.051</i>	0.049 <i>0.735</i>	1.000 <i><0.001</i>	0.575 <i><0.001</i>	0.095 <i>0.462</i>
Average medulla R2*	-0.254	-0.142	-0.252	0.118	0.575	1.000	0.644

Average FSOC medulla	<i>0.045</i>	<i>0.315</i>	<i>0.075</i>	<i>0.414</i>	<i><0.001</i>	<i><0.001</i>	<i><0.001</i>
	-0.290	-0.341	-0.167	0.308	0.095	0.644	1.000
	<i>0.025</i>	<i>0.017</i>	<i>0.257</i>	<i>0.035</i>	<i>0.462</i>	<i><0.001</i>	<i><0.001</i>

Abbreviations: GFR, glomerular filtration rate; RPF, effective renal plasma flow; P_{GLO} , glomerular pressure; RVR, renal vascular resistance; FSOC, furosemide-induced suppression of oxygen consumption; FFA, free fatty acid; M/I, insulin sensitivity index (M-value/mean insulin concentration); DI, disposition index; AIRg, acute insulin response to glucose; ACPRg, acute C-peptide response to glucose; HbA1c, glycated hemoglobin.

Supplemental Figure 1 Study design

Supplemental Figure 1



Supplemental Figure 2 Relationships between insulin secretion and insulin sensitivity in controls with obesity and youth with type 2 diabetes

Supplemental Figure 2

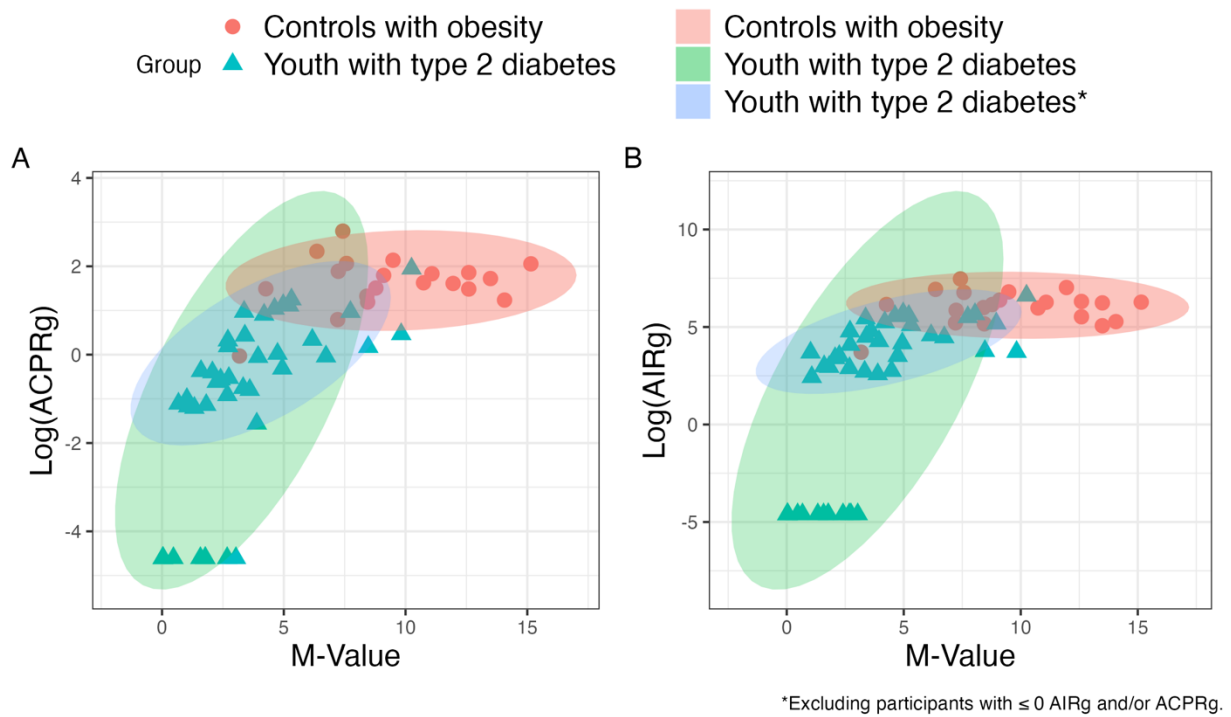
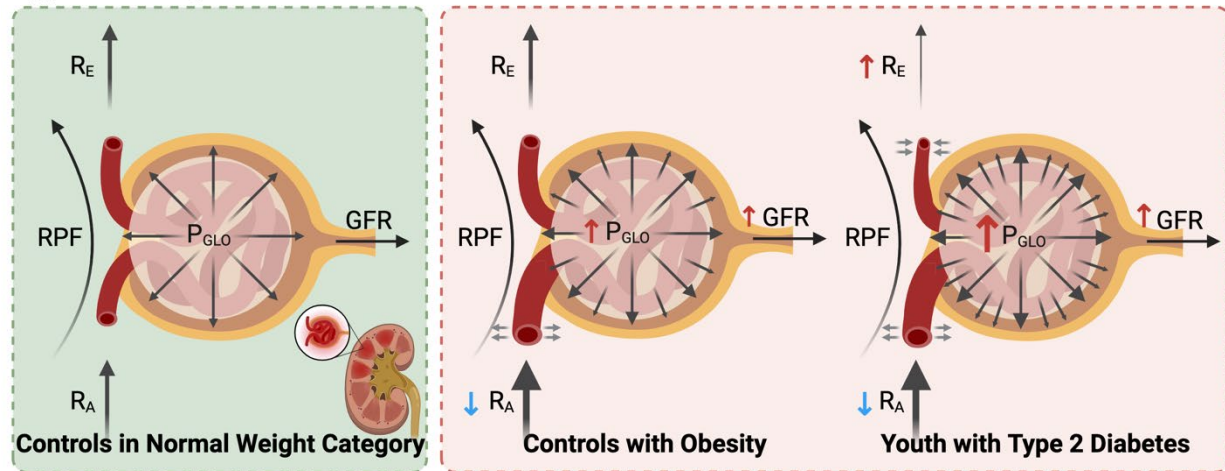


Illustration of relationships between insulin secretion and sensitivity in controls with obesity and youth with type 2 diabetes. Fifteen youth with type 2 diabetes exhibited near-zero AIRg and 8 youth with type 2 diabetes exhibited near-zero ACPRg and were included in the green ellipse. This subset of youths with type 2 diabetes showed negligible insulin and/or c-peptide responses to hyperglycemia, indicating severe β -cell dysfunction. The blue ellipse excludes these participants. Controls with obesity generally maintained consistent insulin secretion across a broad range of insulin sensitivities. In contrast, numerous youths with type 2 diabetes demonstrated both diminished insulin secretion and sensitivity.

Abbreviations: ACPRg, acute C-peptide response to glucose; AIRg, acute insulin response to glucose.

Supplemental Figure 3 Visual illustration of intraglomerular hemodynamic function by group

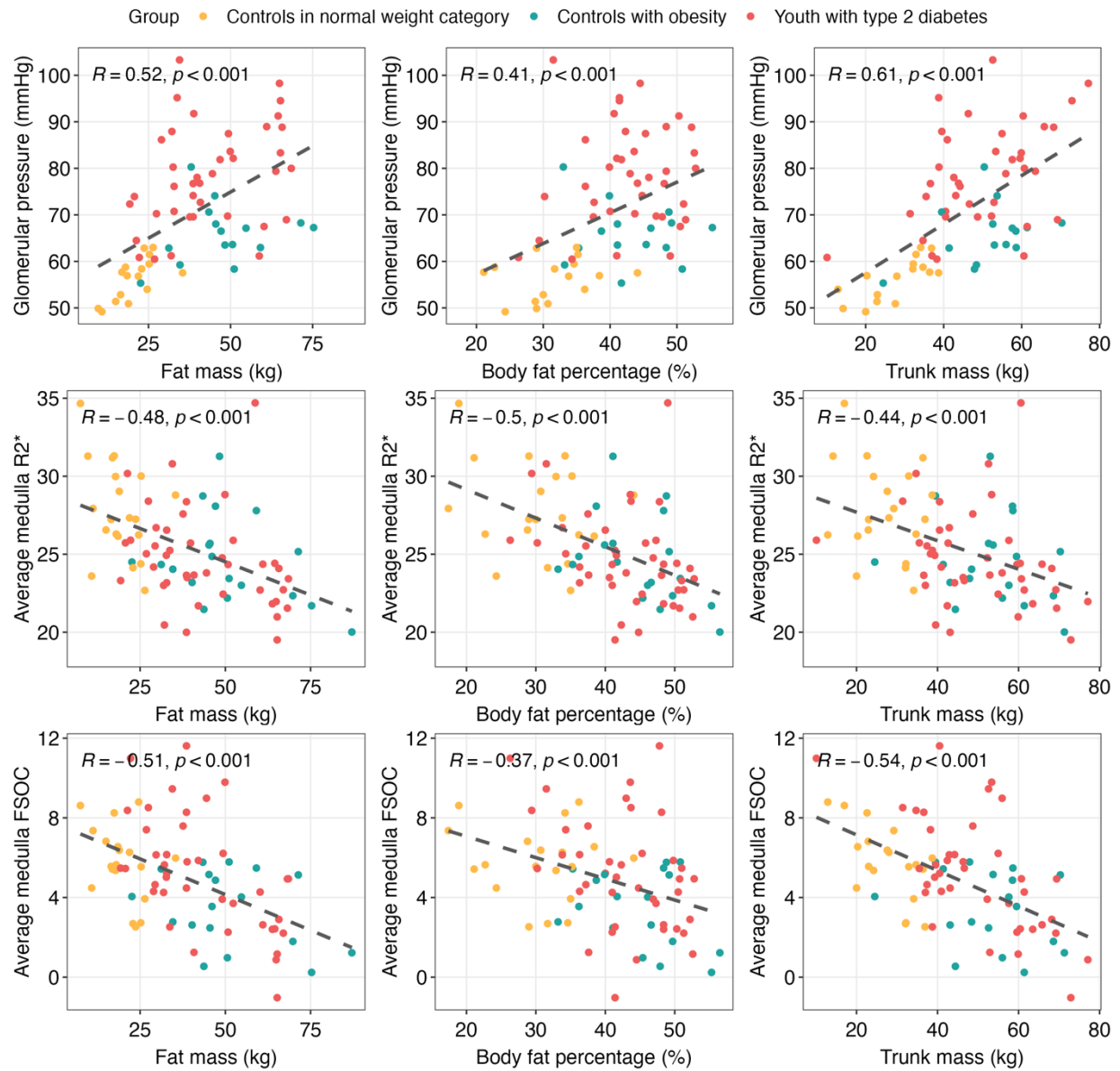
Supplemental Figure 3



Healthy intraglomerular hemodynamic function shown in green box. Intraglomerular hemodynamic function for youth with obesity and type 2 diabetes illustrated based on study findings relative to controls in normal weight category. Up or down arrows indicate a significantly different measure compared to controls in normal weight category ($p < 0.05$). Abbreviations: GFR, glomerular filtration rate; RPF, effective renal plasma flow; P_{GLO} , glomerular pressure; R_A , afferent arteriolar resistance; R_E , efferent arteriolar resistance.

Supplemental Figure 4 Correlation between DXA measures and glomerular pressure, medulla R2* and FSOC by group

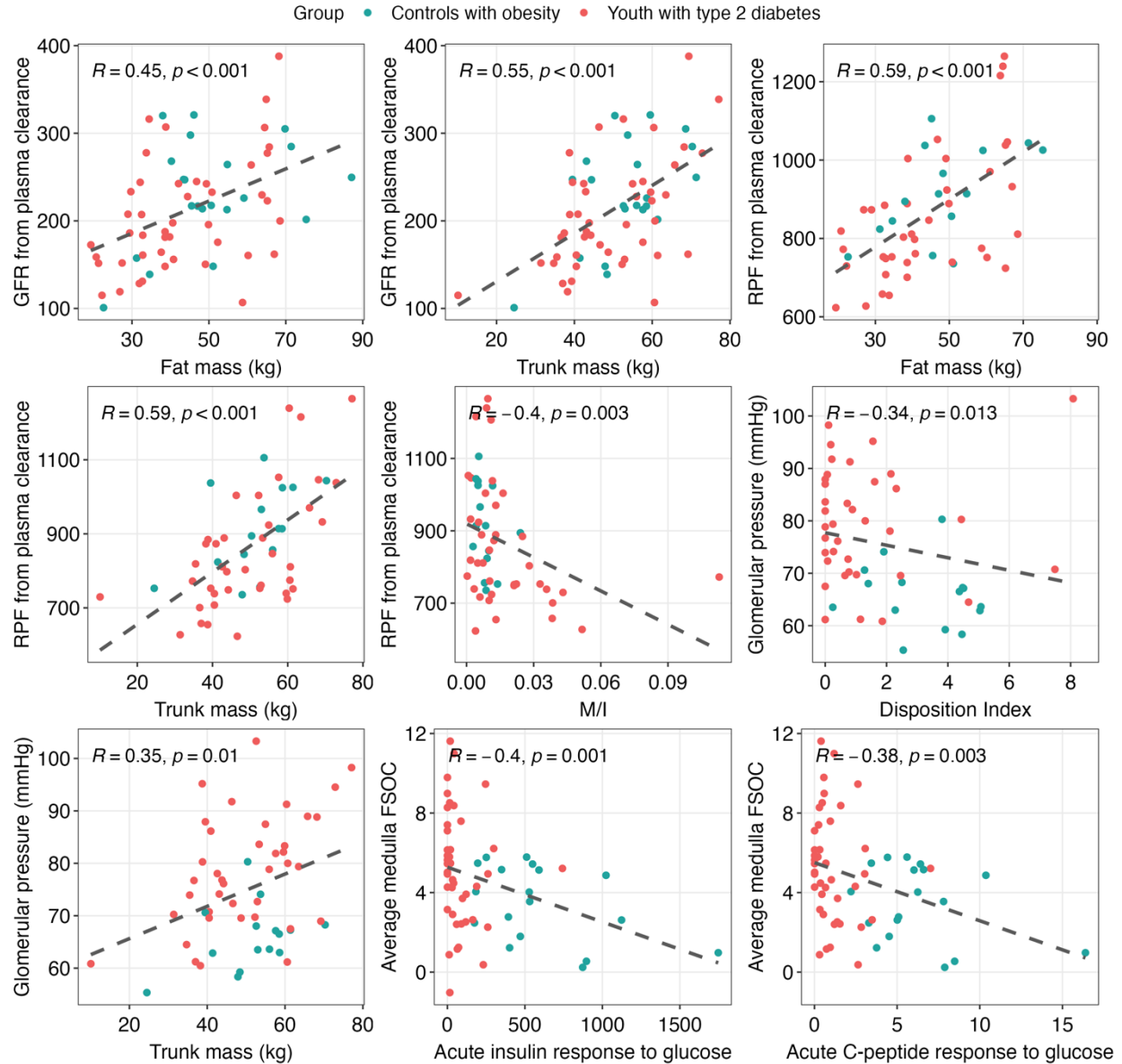
Supplemental Figure 4



Abbreviations: DXA, dual-energy X-ray absorptiometry; FSOC, furosemide-induced suppression of oxygen consumption.

Supplemental Figure 5 Correlation between DXA measures and GFR, DXA measures and RPF, trunk mass and glomerular pressure, glomerular pressure and insulin sensitivity, and FSOC and AIRg and ACPRg in youth with type 2 diabetes and obesity by groups

Supplemental Figure 5



Abbreviations: GFR, glomerular filtration rate; RPF, effective renal plasma flow; FSOC, furosemide-induced suppression of oxygen consumption; FFA, free fatty acid; M/I, insulin sensitivity index (M-value/mean insulin concentration); DI, disposition index.