

Supplemental Table 1. Spearman correlations of activin A with participant characteristics and kidney injury biomarkers

Activin A correlations	Mayo Diabetes Cohort (n=46)		Galway Diabetes Cohort (n=160)		Overall Cohort (n=206)	
	Spearman's Correlation coefficient	p-value	Spearman's Correlation coefficient	p-value	Spearman's Correlation coefficient	p-value
Estimated GFR calculations						
CKD-EPI eGFR, per ml/min/1.73m²	-0.421	0.004	-0.600	0.001	-0.608	<0.0001
MDRD eGFR, per ml/min/1.73m²	-0.416	0.004	-0.586	0.001	-0.595	<0.0001
Cystatin C eGFR, per ml/min/BSA	-0.471	0.001	-	-	-	-
Clinical features and laboratory measurements						
Age, per year	-0.057	0.7	0.348	0.001	0.281	<0.0001
BMI, per kg/m ²	0.227	0.1	0.166	0.04	0.218	0.002
Hemoglobin , per g/L	-0.472	0.001	-0.390	0.001	-0.399	<0.0001
Hemoglobin A _{1c} , per %	0.101	0.5	0.077	0.3	0.094	0.2
Sodium, per mmol/L	0.306	0.04	0.040	0.6	0.137	0.049
Potassium, per mmol/L	0.031	0.8	0.289	0.0002	0.280	<0.0001
Phosphorus, per mg/dL	0.105	0.5	0.194	0.01	0.260	0.0002
Albumin , per g/dL	-0.501	0.0004	-0.392	0.001	-0.473	<0.0001
BUN , per mg/dL	0.318	0.03	0.522	0.001	0.524	<0.0001
PTH , per pg/mL	0.385	0.008	0.462	0.001	0.526	<0.0001
UACR , per mg/g	0.541	0.0002	0.442	0.001	0.479	<0.0001
CRP, mg/L	-0.118	0.4	0.117	0.1	-0.051	0.5
Markers of kidney injury (n=38 plasma; n=37 urine)						
Plasma TNFR-1, per ng/mL	0.627	<0.0001	-	-	-	-
Plasma TNFR-2, per ng/mL	0.436	0.006	-	-	-	-
Plasma KIM-1, per pg/mL	0.554	0.0003	-	-	-	-
Urine Activin A, pg/mL	0.441	0.006	-	-	-	-

Activin A correlations	Mayo Diabetes Cohort (n=46)		Galway Diabetes Cohort (n=160)		Overall Cohort (n=206)	
	Spearman's Correlation coefficient	p-value	Spearman's Correlation coefficient	p-value	Spearman's Correlation coefficient	p-value
Urine Activin A/Creatinine	0.480	0.003	-	-	-	-
Urine MCP-1, pg/mL	0.214	0.2	-	-	-	-
Urine MCP-1/Creatinine	0.339	0.04	-	-	-	-

BMI: body mass index; BUN: blood urea nitrogen; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; eGFR Units: CKD-EPI eGFR (mL/min/1.73m²), MDRD: Modification of Diet Renal Disease (mL/min/1.73m²); Cystatin C (mL/min/BSA); PTH: parathyroid hormone; UACR: urine albumin-creatinine ratio: random sample (Mayo diabetes cohort n=42; Galway n=160); TNFR: tumor necrosis factor receptor; KIM-1: kidney injury marker-1; MCP: monocyte chemoattractant protein-1. NGSP Hb A_{1c} converter <http://www.ngsp.org/convert1.asp> may be used to calculate Hb A_{1c} values from % to mmol/mol.

Supplemental Table 2. Demographic characteristics and clinical laboratory tests by eGFR groups in combined cohorts with diabetes

<i>Characteristic</i>	Overall Diabetes Cohorts					p-value
	eGFR ≥60 (n=92)	eGFR 45-59 (n=27)	eGFR 30-44 (n=53)	eGFR <30 (n=34)	Total (n=206)	
Activin A, pg/mL	326.2 (120.83)	412.4 (148.14)	447.3 (161.11)	626.1 (185.05)	418.1 (180.43)	<.0001
Estimated GFR calculation						
CKD-EPI eGFR, ml/min/1.73m ²	85.8 (15.45)	52.3 (3.67)	36.2 (3.87)	22.6 (4.90)	58.2 (28.22)	<.0001
Clinical features and laboratory measurements						
Age, years	61.3 (10.92)	67.1 (7.05)	71.4 (11.55)	70.2 (10.31)	66.2 (11.43)	<.0001
Female sex, %	25 (27.2%)	5 (18.5%)	18 (34.0%)	12 (35.3%)	60 (29.1%)	0.4
White race/ Irish ethnicity, %	87 (94.6%)	25 (92.6%)	52 (98.1%)	29 (85.3%)	193 (93.7%)	0.1
BMI, kg/m ²	31.8 (5.83)	31.7 (5.77)	31.5 (6.05)	32.8 (5.31)	31.9 (5.77)	0.6
Hemoglobin, g/L	139.14 (13.60)	132.11 (13.01)	126.00 (18.51)	122.24 (16.29)	131.98 (16.79)	<.0001
Hemoglobin A _{1c} , %	7.7 (1.47)	7.5 (1.17)	7.7 (1.29)	8.1 (1.55)	7.7 (1.40)	0.4
Albumin, g/dL	4.5 (0.29)	4.5 (0.30)	4.3 (0.32)	4.2 (0.31)	4.4 (0.33)	<.0001
Creatinine, mg/dL	0.9 (0.20)	1.3 (0.13)	1.7 (0.25)	2.7 (0.71)	1.5 (0.72)	<.0001
BUN, mg/dL	16.6 (5.41)	23.7 (5.43)	32.8 (9.99)	46.9 (15.84)	26.7 (14.39)	<.0001
PTH, pg/mL	31.6 (14.64)	50.4 (28.06)	72.6 (49.85)	107.7 (59.72)	57.2 (46.74)	<.0001
UACR, mg/g	130.6 (429.96)	153.0 (354.60)	333.0 (727.30)	1076.3 (1402.47)	341.0 (813.03)	<.0001
Log UACR	2.9 (1.71)	3.2 (1.91)	4.2 (1.88)	5.6 (2.22)	3.7 (2.10)	<.0001

BMI: body mass index; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate by CKD-EPI equation; PTH: parathyroid hormone; UACR: albumin-creatinine ratio (number per eGFR group; n=91, 25, 53, 33, 202); CRP: C-reactive protein. Values represent mean (standard deviation) or number (%). NGSP Hb A_{1c} converter <http://www.ngsp.org/convert1.asp> may be used to calculate Hb A_{1c} values from % to mmol/mol.

Supplemental Table 3. Demographic characteristics and clinical laboratory tests by tertiles of activin A among cohorts with diabetes

Activin A	Mayo Diabetes Cohort (N=46)				Galway Diabetes Cohort (N=160)			
	Low Tertile (N=15)	Medium Tertile (N=15)	High Tertile (N=16)	P-value trend for Mayo cohort	Low Tertile (N=53)	Medium Tertile (N=55)	High Tertile (N=52)	P-value trend for Galway cohort
Activin A, pg/mL	309.3 (56.47)	487.7 (45.89)	713.7 (136.87)	<.0001¹	246.2 (44.64)	348.3 (29.50)	587.5 (153.07)	<.0001¹
Estimated GFR calculations								
CKD-EPI eGFR	54.0 (20.05)	37.9 (15.03)	32.6 (15.41)	0.005¹	83.7 (22.13)	61.2 (24.32)	44.1 (24.78)	<.0001¹
MDRD eGFR	56.2 (20.89)	40.0 (15.41)	34.2 (15.48)	0.006¹	82.7 (25.07)	61.8 (27.88)	44.2 (25.20)	<.0001¹
Cystatin C eGFR	54.4 (21.00)	34.1 (13.97)	31.1 (13.72)	0.002¹	-	-	-	-
Demographics								
Age, years	67.2 (6.83)	69.7 (4.98)	65.5 (9.14)	0.5 ¹	59.8 (11.35)	68.0 (10.34)	69.6 (13.22)	<.0001¹
Female sex	4 (26.7%)	4 (26.7%)	5 (31.3%)	0.9 ²	12 (22.6%)	17 (30.9%)	18 (34.6%)	0.43 ²
White race	14 (93.3%)	14 (93.3%)	11 (68.8%)	0.09 ²	48(90.6%)	54(98.2%)	52(100%)	0.03²
BMI, kg/m²	33.5 (6.67)	31.7 (4.53)	35.6 (5.11)	0.1 ¹	30.1 (4.51)	31.1 (5.57)	33.1 (6.74)	0.03¹
Clinical laboratory measurements								
Hemoglobin, g/L	138.00 (12.26)	137.00 (14.41)	118.44 (16.24)	0.002¹	140.33 (13.06)	131.61 (17.54)	125.00 (16.09)	<.0001¹
HemoglobinA_{1c}, %	7.7 (1.13)	7.4 (0.90)	8.1 (1.36)	0.5 ¹	7.8 (1.40)	7.4 (1.38)	8.1 (1.56)	0.02¹
Leukocytes, 10⁹/L	6.6 (1.96)	7.4 (2.37)	6.7 (1.93)	0.4 ¹	7.6 (2.34)	7.7 (2.01)	7.9 (2.60)	0.9 ¹
Sodium, mmol/L	138.8 (2.76)	140.4 (2.67)	140.9 (3.42)	0.03¹	139.0 (2.94)	139.7 (2.67)	139.3 (2.74)	0.5 ¹
Potassium, mmol/L	4.7 (0.47)	4.9 (0.50)	4.8 (0.53)	0.6 ¹	4.5 (0.39)	4.6 (0.53)	4.8 (0.45)	0.0007¹
Phosphorus, mg/dL	3.6 (0.43)	3.8 (0.48)	3.9 (1.02)	0.7 ¹	3.2 (0.47)	3.1 (0.57)	3.5 (0.62)	0.002¹
Albumin, g/dL	4.4 (0.31)	4.2 (0.26)	4.0 (0.31)	0.003¹	4.6 (0.26)	4.5 (0.22)	4.3 (0.35)	<.0001¹
BUN, mg/dL	23.8 (7.45)	37.7 (17.01)	36.3 (18.94)	0.02¹	16.9 (7.52)	24.9 (10.59)	33.2 (15.58)	<.0001¹
Creatinine, mg/dL	1.4 (0.44)	1.9 (0.84)	2.3 (0.90)	0.01¹	1.0 (0.31)	1.3 (0.52)	1.8 (0.76)	<.0001¹
PTH, pg/mL	51.0 (31.71)	95.1 (52.57)	98.3 (51.22)	0.01¹	31.6 (16.71)	45.1 (33.54)	74.2 (58.36)	<.0001¹

Activin A	Mayo Diabetes Cohort (N=46)				Galway Diabetes Cohort (N=160)			P-value trend for Galway cohort
	Low Tertile (N=15)	Medium Tertile (N=15)	High Tertile (N=16)	P-value trend for Mayo cohort	Low Tertile (N=53)	Medium Tertile (N=55)	High Tertile (N=52)	
UACR, mg/g	81.7 (176.51)	710.1 (1361.90)	1056.7 (1450.28)	0.005¹	40.4 (91.20)	164.6 (471.35)	598.2 (963.70)	<.0001¹
Log UACR	2.8 (1.72)	4.5 (2.31)	5.5 (2.26)	0.005¹	2.6 (1.33)	3.3 (1.80)	4.8 (2.15)	<.0001¹
CRP, mg/L	3.7 (5.11)	2.0 (4.56)	4.1 (8.60)	0.3 ¹	3.5 (4.27)	4.6 (6.78)	3.9 (4.43)	0.5 ¹
Log CRP	-3.7 (5.76)	-6.3 (5.03)	-5.0 (5.67)	0.3 ¹	0.7 (1.01)	0.9 (1.05)	0.9 (0.97)	0.5 ¹
Markers of kidney injury								
<i>Plasma Biomarkers</i>	12	12	14	38				
TNFR-1, ng/mL	1.6 (0.72)	2.4 (0.83)	3.4 (1.45)	0.0003¹	-	-	-	-
TNFR-2, ng/mL	4.1 (1.55)	5.8 (1.70)	5.9 (1.34)	0.009¹	-	-	-	-
KIM-1, pg/mL	0.2 (0.11)	0.3 (0.31)	0.5 (0.57)	0.004¹	-	-	-	-
<i>Urine Biomarkers</i>	9	14	14	37				
Activin A, pg/mL	0.7 (1.66)	7.6 (14.68)	38.1 (43.40)	0.06 ¹	-	-	-	-
Activin A/Creatinine	0.0 (0.01)	0.1 (0.15)	0.6 (0.72)	0.02¹	-	-	-	-
MCP-1, pg/mL	194.2 (155.94)	149.5 (116.82)	304.0 (321.84)	0.3 ¹	-	-	-	-
MCP-1/Creatinine	1.8 (1.28)	1.8 (1.77)	3.9 (3.37)	0.1 ¹	-	-	-	-

¹Kruskal-Wallis p-value; ²Chi-Square p-value

BMI: body mass index; BUN: blood urea nitrogen; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; eGFR Units: CKD-EPI eGFR (mL/min/1.73m²), MDRD: Modification of Diet Renal Disease (mL/min/1.73m²); Cystatin C (mL/min/BSA); PTH: parathyroid hormone; UACR: urine albumin-creatinine ratio: random sample (Mayo diabetes cohort n=14, 12, 16); TNFR: tumor necrosis factor receptor; KIM-1: kidney injury marker-1; MCP: monocyte chemoattractant protein-1. NGSP HbA_{1c} converter <http://www.ngsp.org/convert1.asp> may be used to calculate HbA_{1c} values from % to mmol/mol. Values represent mean (standard deviation) or number (%).