

Supplemental Table A: Net secretion & CKD correlates – Comparing low (Cat 1), medium (Cat 2), and high (Cat 3) cinnamoylglycine clearance, for subjects with same average Ur-Cr clearance

Characteristics, mean(SD) unless noted	Category 1 (Low) N=98	Category 2 (Medium) N=99	Category 3 (High) N=99	<i>P</i> for <i>trend</i>
Age, years	60.5 (14.5)	59.5 (14.5)	59.0 (12.0)	0.75
Male gender, n(%)	67 (69.1%)	82 (82.8%)	85 (85.0%)	0.01
Black race, n(%)	21 (21.6%)	29 (29.3%)	28 (28.0%)	0.43
Other non-white race, n(%)	13 (13.4%)	8 (8.1%)	6 (6.0%)	0.18
Urea-creatinine clearance, mL/min	54.6 (30.6)	55.1 (38.2)	53.2 (27.7)	0.92
Daily creatinine excretion / lean body mass, mg/kg [†]	31.0 (12.8)	30.8 (12.8)	30.5 (11.0)	0.96
Estimated GFR, mL/min/1.73m ³ [†]	48.3 (28.1)	46.4 (26.7)	47.9 (23.6)	0.87
Body mass index, kg/m ²	31.5 (7.7)	31.5 (7.2)	32.0 (7.7)	0.87
Systolic blood pressure, mmHg	132.6 (22.2)	130.9 (20.7)	129.4 (20.1)	0.55
Current smoking, n(%)	16 (16%)	17 (17%)	24 (24%)	0.29
Current alcohol use, n(%)	23 (23.7%)	32 (32.3%)	39 (39.0%)	0.07
Medications use:				
Aspirin, n(%)	34 (35.1%)	38 (38.4%)	45 (45.0%)	0.35
Statin, n(%)	49 (50.5%)	54 (54.5%)	63 (63.0%)	0.20
H2 blocker, n(%)	8 (8.2%)	10 (10.1%)	9 (9.0%)	0.90
Loop diuretic, n(%)	42 (43.3%)	40 (40.4%)	36 (36.0%)	0.57
Thiazide, n(%)	12 (12.4%)	15 (15.2%)	16 (16.0%)	0.75
ACE inhibitor, n(%)	55 (56.7%)	50 (50.5%)	59 (59.0%)	0.46
Angiotensin-R blocker, n(%)	36 (37.1%)	40 (40.4%)	35 (35.0%)	0.73
Colchicine, n(%)	7 (7.2%)	4 (4.0%)	6 (6.0%)	0.63
EPO, n(%)	3 (3.1%)	6 (6.1%)	4 (4.0%)	0.58
Insulin, n(%)	25 (25.8%)	26 (26.3%)	28 (28.0%)	0.93
Oral diabetes medication, n(%) [†]	21 (21.6%)	18 (18.2%)	21 (21.0%)	0.81
Prevalent diabetes, n(%) [†]	50 (51.5%)	52 (52.5%)	55 (55.0%)	0.88
Prevalent cardiovascular disease, n(%) [†]	8 (8.2%)	12 (12.1%)	5 (5.0%)	0.19
Laboratory measures:				
Hemoglobin A1c, %	6.7 (1.9)	6.4 (1.4)	6.5 (1.2)	0.26
Cholesterol, mg/dL	174.4 (61.5)	176.6 (59.1)	162.8 (44.2)	0.17
C-Reactive Protein, mg/L	5.9 (10.7)	5.1 (6.6)	5.8 (8.0)	0.77
CO2 (bicarbonate), mmol/L	24.5 (3.6)	24.8 (3.7)	25.0 (3.3)	0.60
Fractional excretion Phosphorus, %	29.4 (13.0)	31.4 (16.3)	27.3 (19.0)	0.21
Fractional excretion Uric Acid, %	6.9 (3.9)	7.6 (4.2)	6.5 (6.7)	0.30
Fractional excretion Calcium, %	1.3 (1.3)	1.5 (2.5)	1.1 (1.2)	0.40
Fractional excretion Sodium, %	1.6 (1.4)	1.7 (1.4)	1.5 (1.5)	0.38
Fractional excretion Potassium, %	17.3 (16.5)	14.9 (9.4)	12.5 (7.5)	0.02
Albumin excretion rate, mg/d, med(IQR)	209 (27, 810)	161 (17, 963)	159 (20, 1124)	0.62 [‡]

[†] Oral diabetes medications metformin or sulfonylurea; prevalent diabetes based on self-report, physician diagnosis, use of DM medications, or fasting glucose; cardiovascular disease (CVD) defined as coronary artery disease (CAD), heart failure (HF), peripheral vascular disease (PVD), or cerebrovascular disease (CBVD)

[‡] Test for trend of median AER over categories of clearance based on quantile regression.

Supplemental Table B: Net secretion & CKD correlates – Comparing low (Cat 1), medium (Cat 2), and high (Cat 3) P-cresol sulfate clearance, for subjects with same average Ur-Cr clearance

Characteristics, mean(SD) unless noted	Category 1 (Low) N=95	Category 2 (Medium) N=97	Category 3 (High) N=97	<i>P</i> for <i>trend</i>
Age, years	58.23 (13.71)	59.99 (13.82)	60.86 (14.09)	0.41
Male gender, n(%)	72 (76%)	80 (82%)	75 (77%)	0.50
Black race, n(%)	25 (26%)	23 (24%)	29 (30%)	0.62
Other non-white race, n(%)	7 (7%)	11 (11%)	9 (9%)	0.64
Urea-creatinine clearance, mL/min	52.89 (30.13)	53.43 (32.17)	54.19 (32.01)	0.96
Daily creatinine excretion / lean body mass, mg/kg [†]	29.85 (11.52)	30.48 (11.14)	31.18 (13.42)	0.75
Estimated GFR, mL/min/1.73m ³ [†]	48.26 (27.85)	45.83 (24.88)	47.88 (26.38)	0.79
Body mass index, kg/m ²	31.03 (7.34)	31.96 (7.74)	31.99 (7.72)	0.61
Systolic blood pressure, mmHg	129.65 (20.64)	129.81 (19.26)	134.46 (23.27)	0.20
Current smoking, n(%)	17 (18%)	18 (19%)	20 (21%)	0.90
Current alcohol use, n(%)	34 (36%)	31 (32%)	25 (26%)	0.32
Medications use:				
Aspirin, n(%)	32 (34%)	42 (43%)	43 (44%)	0.25
Statin, n(%)	49 (52%)	58 (60%)	56 (58%)	0.49
H2 blocker, n(%)	11 (12%)	8 (8%)	7 (7%)	0.54
Loop diuretic, n(%)	34 (36%)	40 (41%)	45 (46%)	0.33
Thiazide, n(%)	14 (15%)	12 (12%)	15 (15%)	0.81
ACE inhibitor, n(%)	56 (59%)	55 (57%)	52 (54%)	0.76
Angiotensin-R blocker, n(%)	31 (33%)	39 (40%)	40 (41%)	0.41
Colchicine, n(%)	4 (4%)	10 (10%)	3 (3%)	0.07
EPO, n(%)	4 (4%)	3 (3%)	6 (6%)	0.57
Insulin, n(%)	25 (26%)	25 (26%)	29 (30%)	0.78
Oral diabetes medication, n(%) [†]	17 (18%)	19 (20%)	22 (23%)	0.70
Prevalent diabetes, n(%) [†]	53 (56%)	49 (51%)	53 (55%)	0.74
Prevalent cardiovascular disease, n(%) [†]	5 (5%)	13 (13%)	7 (7%)	0.11
Laboratory measures:				
Hemoglobin A1c, %	6.42 (1.42)	6.57 (1.56)	6.63 (1.56)	0.61
Cholesterol, mg/dL	180.38 (59.69)	168.60 (57.78)	165.36 (49.49)	0.15
C-Reactive Protein, mg/L	5.03 (7.24)	5.87 (9.09)	5.52 (8.53)	0.78
CO2 (bicarbonate), mmol/L	23.88 (3.80)	25.07 (3.18)	25.44 (3.39)	0.01
Fractional excretion Phosphorus, %	31.22 (20.97)	29.94 (15.67)	27.15 (11.32)	0.22
Fractional excretion Uric Acid, %	7.76 (7.39)	7.23 (3.94)	6.11 (2.95)	0.08
Fractional excretion Calcium, %	1.65 (2.85)	1.21 (0.92)	1.02 (0.97)	0.05
Fractional excretion Sodium, %	1.90 (1.90)	1.64 (1.23)	1.31 (0.91)	0.01
Fractional excretion Potassium, %	15.34 (13.66)	15.52 (12.23)	14.43 (9.74)	0.79
Albumin excretion rate, mg/d, med(IQR)	70.73 (36.84)	63.82 (29.76)	60.19 (43.64)	0.14

[†] Oral diabetes medications metformin or sulfonylurea; prevalent diabetes based on self-report, physician diagnosis, use of DM medications, or fasting glucose; cardiovascular disease (CVD) defined as coronary artery disease (CAD), heart failure (HF), peripheral vascular disease (PVD), or cerebrovascular disease (CBVD)

‡ Test for trend of median AER over categories of clearance based on quantile regression.

Supplemental Table C: Net secretion & CKD correlates – Comparing low (Cat 1), medium (Cat 2), and high (Cat 3) Indoxyl sulfate clearance, for subjects with same average Ur-Cr clearance

Characteristics, mean(SD) unless noted	Category 1 (Low) N=95	Category 2 (Medium) N=98	Category 3 (High) N=96	<i>P for trend</i>
Age, years	57.40 (14.14)	60.57 (14.80)	60.86 (12.47)	0.16
Male gender, n(%)	70 (74%)	84 (86%)	73 (76%)	0.10
Black race, n(%)	22 (23%)	21 (21%)	33 (34%)	0.09
Other non-white race, n(%)	8 (8%)	13 (13%)	6 (6%)	0.23
Urea-creatinine clearance, mL/min	53.77 (33.73)	53.55 (32.15)	54.27 (31.64)	0.99
Daily creatinine excretion / lean body mass, mg/kg [†]	29.52 (11.27)	31.70 (11.41)	30.68 (13.82)	0.46
Estimated GFR, mL/min/1.73m ³ [†]	49.79 (30.00)	43.58 (24.08)	48.85 (24.74)	0.21
Body mass index, kg/m ²	31.08 (7.21)	30.67 (7.27)	33.10 (8.07)	0.06
Systolic blood pressure, mmHg	129.95 (21.37)	130.56 (19.47)	133.40 (22.49)	0.48
Current smoking, n(%)	16 (17%)	19 (19%)	21 (22%)	0.72
Current alcohol use, n(%)	35 (37%)	31 (32%)	26 (27%)	0.35
Medications use:				
Aspirin, n(%)	31 (33%)	35 (36%)	51 (53%)	0.01
Statin, n(%)	49 (52%)	53 (54%)	60 (63%)	0.28
H2 blocker, n(%)	11 (12%)	8 (8%)	7 (7%)	0.55
Loop diuretic, n(%)	31 (33%)	38 (39%)	49 (51%)	0.03
Thiazide, n(%)	11 (12%)	16 (16%)	14 (15%)	0.63
ACE inhibitor, n(%)	58 (61%)	50 (51%)	53 (55%)	0.37
Angiotensin-R blocker, n(%)	30 (32%)	41 (42%)	38 (40%)	0.31
Colchicine, n(%)	6 (6%)	7 (7%)	4 (4%)	0.66
EPO, n(%)	4 (4%)	4 (4%)	5 (5%)	0.92
Insulin, n(%)	23 (24%)	25 (26%)	30 (31%)	0.51
Oral diabetes medication, n(%) [†]	16 (17%)	15 (15%)	28 (29%)	0.03
Prevalent diabetes, n(%) [†]	48 (51%)	49 (50%)	57 (59%)	0.34
Prevalent cardiovascular disease, n(%) [†]	4 (4%)	14 (14%)	7 (7%)	0.04
Laboratory measures:				
Hemoglobin A1c, %	6.31 (1.46)	6.43 (1.44)	6.84 (1.59)	0.04
Cholesterol, mg/dL	180.40 (58.77)	165.93 (56.36)	167.09 (51.64)	0.14
C-Reactive Protein, mg/L	5.21 (7.32)	4.72 (8.17)	6.52 (9.29)	0.30
CO2 (bicarbonate), mmol/L	23.97 (3.70)	24.74 (3.54)	25.58 (3.13)	0.01
Fractional excretion Phosphorus, %	30.14 (21.10)	33.37 (15.72)	25.13 (9.96)	<0.01
Fractional excretion Uric Acid, %	7.87 (7.67)	7.30 (3.39)	5.92 (2.84)	0.03
Fractional excretion Calcium, %	1.68 (2.87)	1.21 (0.90)	0.97 (0.92)	0.02
Fractional excretion Sodium, %	1.85 (1.89)	1.77 (1.29)	1.24 (0.82)	0.01
Fractional excretion Potassium, %	15.13 (13.96)	16.26 (12.63)	13.84 (8.62)	0.37
Albumin excretion rate, mg/d, med(IQR)	68.84 (37.71)	68.83 (31.18)	56.73 (41.49)	0.03

[†] Oral diabetes medications metformin or sulfonylurea; prevalent diabetes based on self-report, physician diagnosis, use of DM medications, or fasting glucose; cardiovascular disease (CVD) defined as coronary artery disease (CAD), heart failure (HF), peripheral vascular disease (PVD), or cerebrovascular disease (CBVD)

‡ Test for trend of median AER over categories of clearance based on quantile regression.

Supplemental Table D: Net secretion and events comparing categories of solute clearance relative to average Urea-Creatinine clearance, with adjustment for AER			
	Number of events	Incidence / 100 py (95% CI) [†]	Hazard ratio (95% CI) [‡]
(A) Hippurate			
Outcome: Death			
HA: Low (vs. High)	19	6.8 (3.8, 9.9)	2.5 (1.2, 5.5)
HA: Medium (vs High)	12	4.4 (2.1, 7.0)	1.1 (0.5, 2.5)
HA: High (<i>Referent</i>)	11	3.8 (1.8, 6.6)	<i>Reference</i>
Outcome: Dialysis [†]			
HA: Low (vs. High)	7	2.7 (0.9, 4.8)	1.5 (0.3, 6.7)
HA: Medium (vs High)	7	2.6 (0.9, 4.8)	1.1 (0.4, 3.0)
HA: High (<i>Referent</i>)	6	2.1 (0.7, 4.4)	<i>Reference</i>
(B) Cinnamoylglycine			
Outcome: Death [†]			
CMG: Low (vs High)	12	4.4 (2.1, 7.0)	1.0 (0.5, 2.1)
CMG: Medium (vs High)	16	5.8 (3.1, 8.7)	1.0 (0.5, 2.1)
CMG: High (<i>Referent</i>)	15	5.1 (2.8, 8.3)	<i>Reference</i>
Outcome: Dialysis [†]			
CMG: Low (vs High)	9	3.5 (1.4, 5.7)	3.3 (0.7, 15.7)
CMG: Medium (vs High)	6	2.3 (0.7, 4.4)	1.1 (0.3, 4.6)
CMG: High (<i>Referent</i>)	4	1.4 (0.4, 3.4)	<i>Reference</i>
(C) P-cresol sulfate			
Outcome: Death [†]			
PCS: Low (vs High)	14	5.6 (3.3, 9.4)	2.5 (1.0, 6.1)
PCS: Medium (vs High)	17	6.0 (3.7, 9.6)	1.3 (0.6, 3.1)
PCS: High (<i>Referent</i>)	11	4.0 (2.2, 7.2)	<i>Reference</i>
Outcome: Dialysis [†]			
PCS: Low (vs High)	9	3.8 (2.0, 7.3)	0.9 (0.2, 4.0)
PCS: Medium (vs High)	7	2.5 (1.2, 5.3)	1.3 (0.3, 5.4)
PCS: High (<i>Referent</i>)	4	1.5 (0.6, 3.9)	<i>Reference</i>
(D) Indoxyl sulfate			
Outcome: Death [†]			
IS: Low (vs High)	12	4.8 (2.7, 8.4)	1.1 (0.5, 2.5)
IS: Medium (vs High)	14	4.8 (2.8, 8.0)	0.6 (0.3, 1.3)
IS: High (<i>Referent</i>)	16	6.0 (3.7, 9.8)	<i>Reference</i>
Outcome: Dialysis [†]			
IS: Low (vs High)	9	3.8 (2.0, 7.4)	1.1 (0.2, 7.1)
IS: Medium (vs High)	8	2.8 (1.4, 5.6)	1.8 (0.3, 9.7)
IS: High (<i>Referent</i>)	3	1.1 (0.4, 3.5)	<i>Reference</i>

[†] 95% confidence intervals calculated from Poisson distribution.

[‡] Cox proportional hazards models, comparing categories of net tubular solute clearance; adjusted for age, sex, black race, other non-white race, albumin excretion rate (AER), and Ur-Cr clearance.