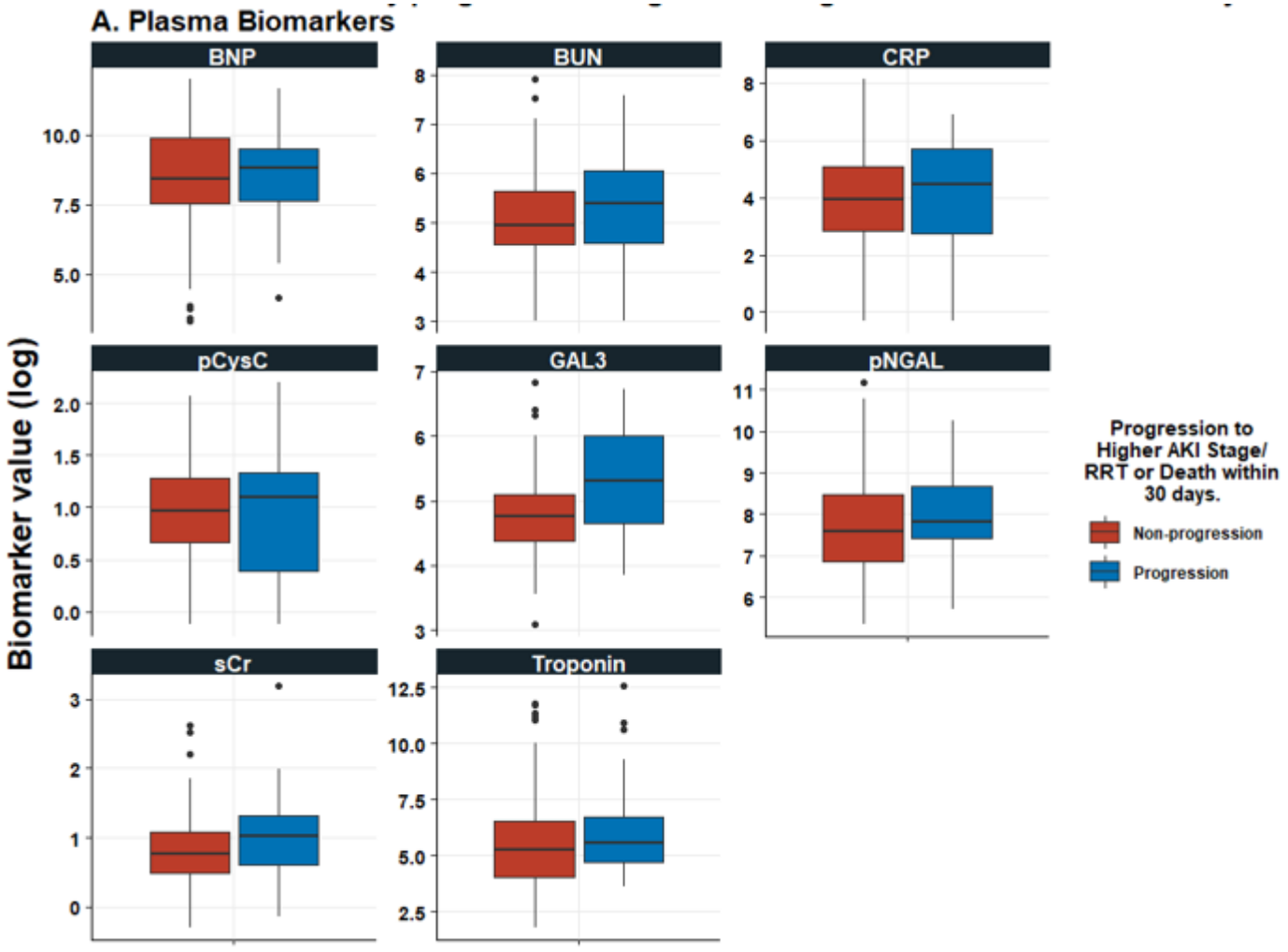
SUPPLEMENTAL MATERIAL

Supplemental Statistical Methods

Odds ratios were used for the primary analysis due to the ease of interpretability and a non-linear sensitivity analysis was also conducted. Non-linearity of biomarkers was assessed by fitting 3-4 restricted cubic splines, using the rms package in R, and the Wald test of the non-linear coefficient was also calculated. Biomarkers were considered non-linear if they had a significant p-value for the Wald test and the model fit was improved by a decrease in the Akaike information criterion (AIC) of >2. The Chi square statistic of the "pre-test" logistic regression clinical model, composed of the adjustment variables, was compared with the "post-test" clinical model after the addition of the biomarker of interest using the likelihood-ratio test. Localized non-parametric regression using the loess function from the *Hmisc* package in R was used to graphically represent estimated probabilities versus biomarker levels to assist in the interpretation of the non-linear relationships.

Supplemental Figures

Figure S1. Distribution of (A) plasma and (B) urinary biomarkers at the time of WRF stage 1-2 diagnosis within 72 hours of hospital admission stratified by progression to the primary composite outcome within 30 days.



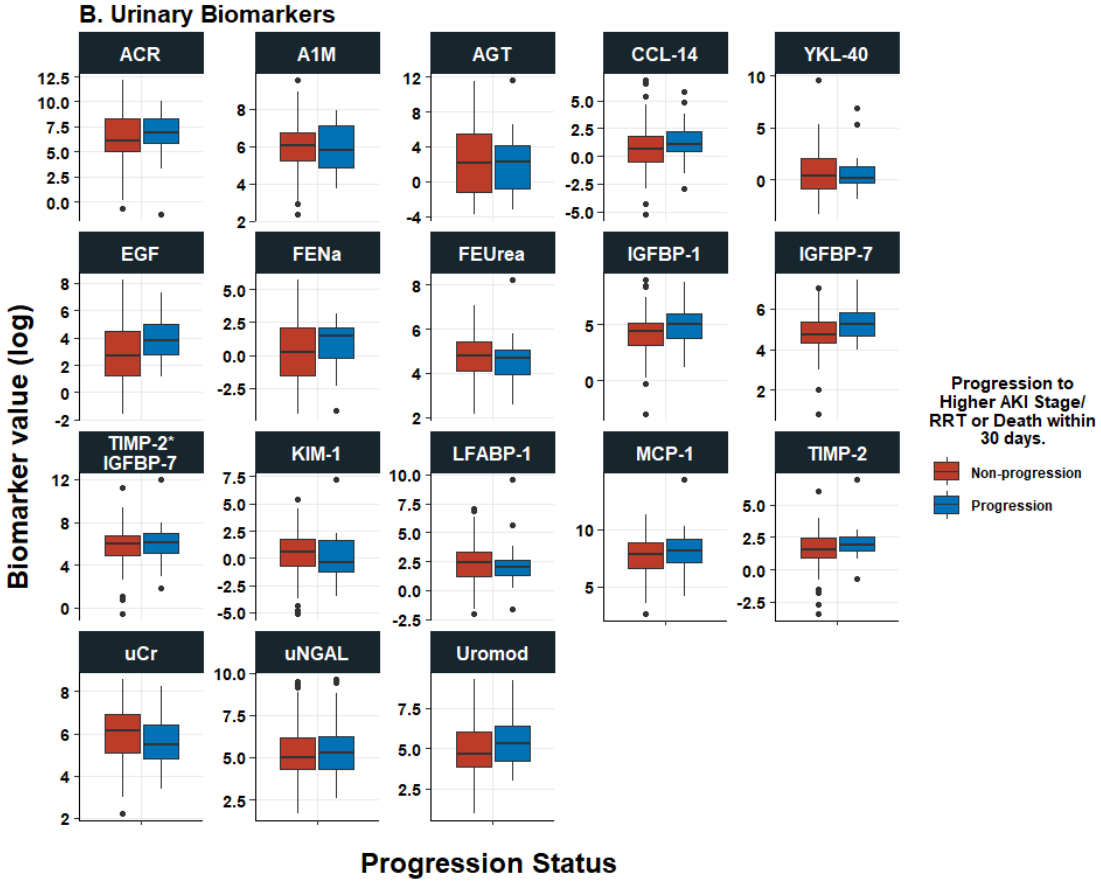

B. Urinary Biomarkers
ACR
A1M
AGT
CCL-14
YKL-40
EGF
FENa
FEUrea
IGFBP-1
IGFBP-7
TIMP-2* IGFBP-7
KIM-1
LFABP-1
MCP-1
TIMP-2
uCr
uNGAL
Uromod
Biomarker value (log)
Progression Status
Progression to Higher AKI Stage/ RRT or Death within 30 days.
Non-progression
Progression

Figure S2. Distribution of (A) plasma and (B) urinary biomarkers at the time of WRF stage 1-2 diagnosis within 72 hours of hospital admission stratified by progression to a higher WRF Stage or RRT within 30 days.

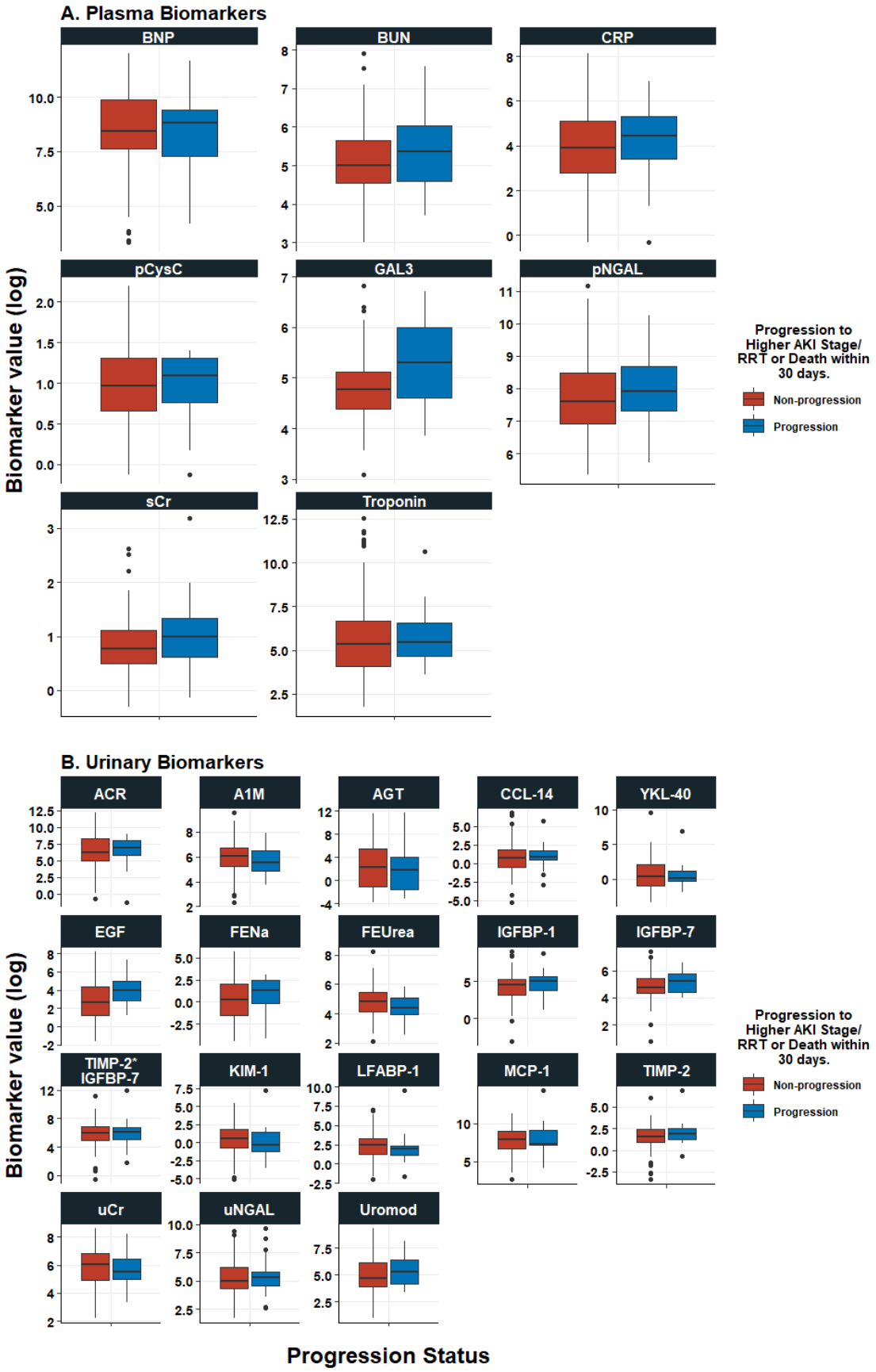


Figure S3. Odds ratio of the highest biomarker tertile versus the lowest biomarker tertile for progression to higher stage of worsening renal function or renal replacement therapy within 30 days after adjusting for systolic blood pressuree and BUN.

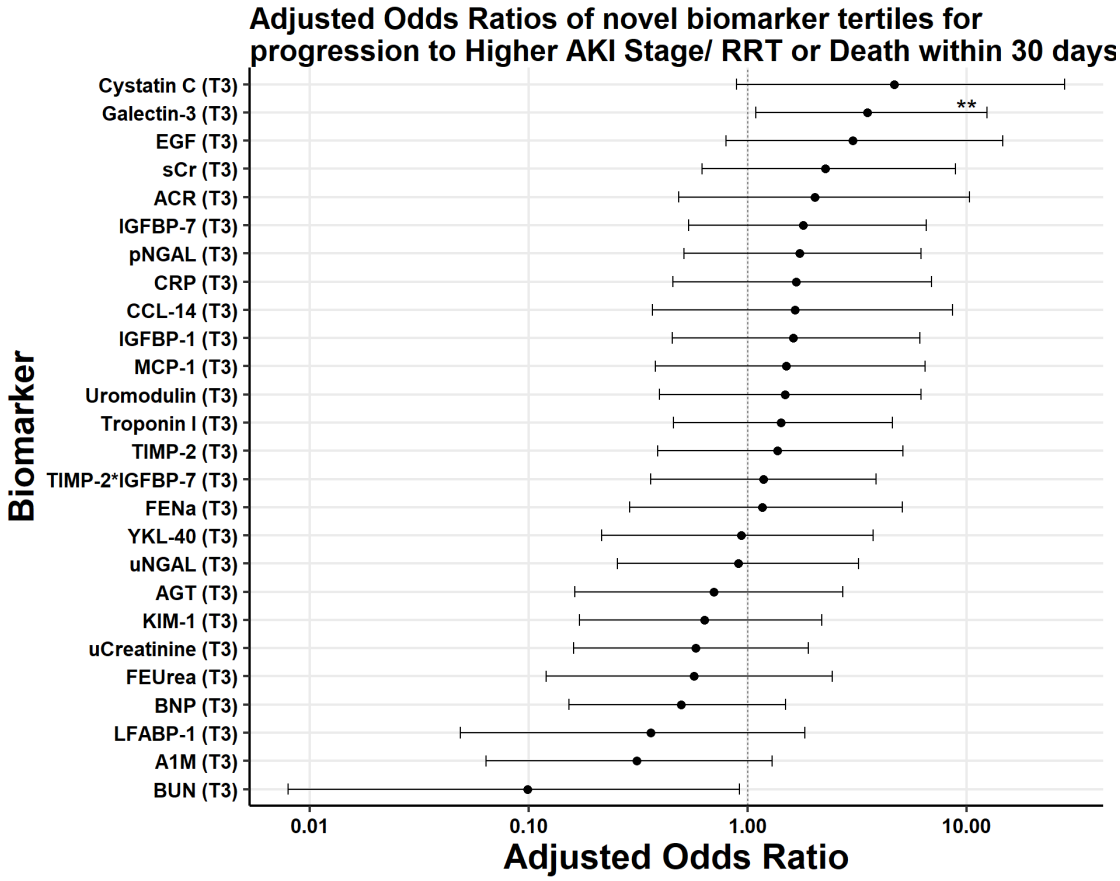


Figure Legends

Figure S1

Abbreviations: ACR, Albumin to creatinine ratio;A1M, alpha 1-microglobulin; uAGT, urinary angiotensinogen; BNP, brain natriuretic peptide; CCL-14, C-C motif chemokine ligand 14; CRP, C-reactive protein; IGFBP-1, EGF, Epidermal Growth Factor; FENa, Fractional Excretion of Sodium; FEUrea, Fractional Excretion of Urea; Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; KIM-1, kidney injury molecule-1; L-FABP-1, liver-type fatty acid–binding protein-1; MCP-1, monocyte chemotactic protein-1; pNGAL, plasma neutrophil gelatinase–associated lipocalin; RRT, Renal Replacement Therapy; TIMP-2, tissue inhibitor of metalloproteinases-2; uNGAL, urinary neutrophil gelatinase–associated lipocalin; YKL-40, chitinase-3-like protein 1**;** uCr, urinary creatinine.

Figure S2

Abbreviations: ACR, Albumin to creatinine ratio;A1M, alpha 1-microglobulin; uAGT, urinary angiotensinogen; BNP, brain natriuretic peptide; CCL-14, C-C motif chemokine ligand 14; CRP, C-reactive protein; IGFBP-1, EGF, Epidermal Growth Factor; FENa, Fractional Excretion of Sodium; FEUrea, Fractional Excretion of Urea; Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth

factor-binding protein 7; KIM-1, kidney injury molecule-1; L-FABP-1, liver-type fatty acid–binding protein-1; MCP-1, monocyte chemotactic protein-1; pNGAL, plasma neutrophil gelatinase–associated lipocalin; RRT, Renal Replacement Therapy; TIMP-2, tissue inhibitor of metalloproteinases-2; uNGAL, urinary neutrophil gelatinase–associated lipocalin; YKL-40, chitinase-3-like protein 1; uCreatinine, urinary creatinine.

Figure S3

** p-value <0.05

Abbreviations: A1M, alpha 1-microglobulin; ACR, Albumin to Creatinine Ratio; AGT, angiotensinogen; BNP, brain natriuretic peptide; CCL-14, chemokine ligand 14; CRP, C-reactive protein; EGF, epidermal growth factor; FeNa, fractional excretion of sodium; FeUrea, fractional excretion of urea; IGFBP-1, Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; L-FABP-1, KIM-1, kidney injury molecule-1; LFABP-1, liver-type fatty acid–binding protein-1; MCP-1, monocyte chemotactic protein-1; pNGAL, plasma neutrophil gelatinase–associated lipocalin; sCreatinine, serum creatinine TIMP-2, tissue inhibitor of metalloproteinases-2; uNGAL, urine neutrophil gelatinase–associated lipocalin; YKL-40, chitinase-3-like protein 1**;** uCreatinine, urinary creatinine.

Supplemental Tables

Table S1. Percentage of specimens available on the day of AKI/WRF Diagnosis versus within 24 hours of criteria.

Biomarker	Specimen on the Day Of AKI/WRF	Specimen Within 24 Hours of AKI/WRF
BNP	85.1%	14.9%
hs-cTnI	81.1%	18.9%
Galectin-3	85.7%	14.3%
Plasma NGAL	85.7%	14.3%
Urine NGAL	83.9%	16.1%
KIM-1	89.9%	10.1%
EGF	89.9%	10.1%
Cystatin C	86.4%	13.4%
CCL-14	89.9%	10.1%
IGFBP-7	89.9%	10.1%
IGFBP-1	89.9%	10.1%
ACR	90.7%	9.3%
AGT	89.2%	10.8%
MCP-1	89.9%	10.1%
TIMP-2	89.2%	10.8%
A1M	89.9%	10.1%
LFABP-1	89.2%	10.8%
Uromodulin	89.9%	10.1%
CRP	87.4%	12.6%
YKL-40	89.9%	10.1%
Urine Sodium	88.4%	11.6%
Urine Urea	87.5%	12.4%

Abbreviations: AKI, acute kidney injury; ACR, Albumin to Creatinine Ratio; BNP, B-type natriuretic peptide; hs-cTnI, high-sensitivity cardiac troponin I; NGAL, neutrophil gelatinase-associated lipocalin; L-FABP-1, liver-type fatty acid–binding protein-1; KIM-1, kidney injury molecule-1; AGT, urinary angiotensinogen; A1M, alpha 1-microglobulin; YKL-40, chitinase-3-like protein 1; MCP-1, monocyte chemotactic protein-1; TIMP-2, tissue inhibitor of metalloproteinases-2; IGFBP-1, Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; WRF, worsening renal function

Table S2: Details of assay manufacturers, measurement range and accuracy.

Biomarker	Assay Type	Sample Type	Manufacturer	Sensitivity*	Measurement Range	Inter-assay CV	Intra-assay CV†
Galectin-3	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	1.0 ng/mL	5.5 to 103.1 ng/mL	≤ 4.8%	≤ 4.2%
Cystatin C	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	0.031 mg/L	0.27-8.8 mg/L	≤ 3.54%	≤ 1.93%
Galectin-3	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	1 ng/ml	5.5 to 103.1 ng/mL.	≤ 4.2%	≤ 4.8%
hs-cTnI	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	1.9 ng/L	2.7 to 3600.0 ng/L	≤ 3.9%	≤ 6.2%
BNP	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	10 ng/L	10 to 5000 pg/mL.	≤ 6.7%	≤ 5.6%
CRP	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	0.2 mg/L	0.2 – 320 mg/L	≤ 1.4%	≤ 2.1%
Sodium	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	0.53 mmol/l	115 - 164 mmol/l	≤ 1.6%	≤ 1.6%
Urea	Architect	Plasma	Abbott Diagnostic, Wiesbaden, Germany	0.25 mmol/L	0.5 - 46 mmol/l	≤ 3%	≤ 3%
Sodium	Architect	Urine	Abbott Diagnostic, Wiesbaden, Germany	0.48 mmol/l	2 - 275 mmol/l	≤ 1.6%	≤ 1.6%
Urea	Architect	Urine	Abbott Diagnostic, Wiesbaden, Germany	5.4 mmol/L	0.8 - 35.5 mmol/l	≤ 3%	≤ 3%
Albumin	Architect	Urine	Abbott Diagnostic, Wiesbaden, Germany	0.3 g/dL	0.3 – 9.4 g/dL	≤ 1.5%	≤ 1.3%
pNGAL	Alere	Plasma	Alere Inc, San Diego, California	0.7 ng/ml	15-1300 ng/mL	≤ 2.1%	≤ 2.1%
uNGAL	Architect	Urine	Abbott Diagnostic, Wiesbaden, Germany	≤ 1 ng/ml	10 - 6000 ng/mL.	≤ 6.7%	≤ 5.2%
ELISA Assays							
LFABP-1	ELISA	Urine	CMIC Holdings Ltd., Tokyo, Japan	0.3 ng/mL	0.3 - 60 ng/mL	≤ 4.1%	<15%
Angiotensinogen	ELISA	Urine	IBL Co., Ltd., Fujioka-Shi, Japan	0.03 ng/mL	0.31 - 20 ng/mL	≤ 5.8%	≤ 5.5%
TIMP-2	ELISA	Urine	R&D Systems (Minneapolis, MN, USA)	0.011 ng/mL	2.61-6.33 µg/g creatinine	≤ 7.8%	≤ 6.5%
Uromodulin	ELISA	Urine	MD Bioproducts, Zurich, Switzerland	< 1 ng/mL	2.3 ng/ml - 150 ng/ml	≤ 12.9%	≤ 8.8%
EGF	ELISA	Urine	R&D Systems (Minneapolis, MN, USA)	0.7 pg/mL	3.9 - 250 pg/mL	≤ 6%	≤ 4.5%
CCL-14	ELISA	Urine	Thermo Fisher, Waltham, MA, USA	7 pg/mL	6.14-1500 pg/mL	<12%	<10%
Luminex Assays							
A1M	Luminex	Urine	R&D Systems (Minneapolis, MN, USA)	29563 pg/mL	147,826 - 35,921,60 pg/mL	<25%	≤ 17.6%
MCP-1	Luminex	Urine	R&D Systems (Minneapolis, MN, USA)	9.9 pg/mL	33-8,017 pg/mL	<25%	≤ 6.3%
YKL-40	Luminex	Urine	R&D Systems (Minneapolis, MN, USA)	3.3 pg/mL	352 - 85,610 pg/mL	<25%	≤ 3.9%
IGFBP-1	Luminex	Urine	R&D Systems (Minneapolis, MN, USA)	42.6 pg/mL	139 - 33,690 pg/mL	<25%	≤ 5.3%
IGFBP-7	Luminex	Urine	R&D Systems (Minneapolis, MN, USA)	118 pg/mL	385 - 93,600 pg/mL	<25%	≤ 5%
KIM-1	Luminex	Urine	R&D Systems (Minneapolis, MN, USA)	17.3 pg/mL	100 - 24,370 pg/mL	<25%	≤ 12%

*For the Architect and Alere assays, the Limit of Detection is provided as a measure of the assay sensitivity; †Intra-assay CV values are provided from the manufacturer except for the Luminex assays where the analysed intra-assay values are provided. The manufacturer advises that the maximum intra-assay CV is <20% but real world values are typically much lower.

Abbreviations: CV, Coefficient of Variation; NA, not applicable; BNP, brain natriuretic peptide; uCr, urinary creatinine; pNGAL, plasma neutrophil gelatinase associated lipocalin; uNGAL, urinary neutrophil gelatinase associated lipocalin; L-FABP-1, liver-type fatty acid binding protein-1; KIM-1, kidney injury molecule-1; KIM-1, kidney injury molecule 1; uAGT, urinary angiotensinogen; A1M, alpha 1-microglobulin; YKL-40, chitinase-3-like protein 1; MCP-1, monocyte chemotactic protein-1; TIMP-2, tissue inhibitor of metalloproteinases-2; IGFBP-1, Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; ACR, Albumin to creatinine ratio; pCysC, plasma Cystatin C; CRP, C-reactive protein; EGF, Epidermal Growth Factor; CCL-14, C-C motif chemokine ligand 14

Table S3. Admission Characteristics for patients with Stage 1-2 WRF within 72 hours of admission stratified by progression to higher WRF Stage or RRT within 30 days.

n n	**N**	**Non-progressor** 151	**Progressor** 24	p-value
Age (mean (SD))	175	69.5 (12.7)	69.3 (18.7)	0.934
Male (%)	175	97 (64.2)	11 (45.8)	0.113
Black ethnicity (%)	175	49 (32.5)	10 (41.7)	0.486
Heart rate, beats/min (mean (SD))	175	87.4 (21.8)	91.1 (16.8)	0.427
Systolic blood pressure, mm Hg (mean (SD))	175	145.8 (30.7)	139.5 (33.0)	0.358
Diastolic blood pressure, mm Hg (mean (SD))	175	81.8 (22.3)	80.9 (22.0)	0.850
Coronary artery disease (%)	175	83 (55.0)	13 (54.2)	1.00
Hypertension (%)	175	128 (84.8)	20 (83.3)	0.769
Cerebrovascular accident (%)	175	24 (15.9)	2 (8.3)	0.537
Peripheral arterial disease (%)	175	3 (2.0)	0 (0.0)	1.000
COPD (%)	175	34 (22.5)	8 (33.3)	0.303
Chronic kidney disease (%)	175	43 (28.5)	12 (50.0)	0.056
Tobacco use (%)	175	24 (15.9)	2 (8.3)	0.537
Diabetes (%)	175	83 (55.0)	12 (50.0)	0.666
Hyperlipidemia (%)	175	86 (57.0)	14 (58.3)	1.000
Beta-blockers (%)	175	114 (75.5)	15 (62.5)	0.213
ACE inhibitors (%)	175	67 (44.4)	10 (41.7)	0.829
Diuretics (%)	175	94 (62.3)	18 (75.0)	0.260
Angiotensin-receptor blockers (%)	175	29 (19.2)	7 (29.2)	0.281
Antiarrhythmic agent (%)	175	22 (14.6)	5 (20.8)	0.541
Hemoglobin, g/dl (median [IQR])	175	11.2 [9.3, 13.1]	10.5 [9.1, 11.7]	0.196
BUN, mg/dl (median [IQR])	175	25.0 [18.6, 40.8]	24.5 [19.1, 53.2]	0.714
Sodium, mmol/l (median [IQR])	175	139.0 [136.0, 142.0]	139.0 [136.0, 140.2]	0.241
eGFR, ml/min/1.73 m2 (median [IQR])	175	50.8 [37.6, 69.2]	48.1 [30.9, 68.0]	0.564

ACE, angiotensin converting enzyme; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IQR, inter-quartile range; PCI, Percutaneous coronary intervention; SD, standard deviation

Table S4 Median, First and Third Quartile Values for Progressors versus Non-Progressors to the Primary Composite Outcome Measured at Time of Worsening Renal Function in Acute Heart Failure Hospitalization

Biomarker	Non-progressor n=143	Progressor n=143	p-value
Serum/Plasma Biomarkers			
Galectin-3 (ng/ml) (median [IQR])	26.9 [20.6, 34.0]	39.5 [25.0, 63.7]	**<0.001**
NGAL (ng/ml) (median [IQR])	194.0 [117.7, 358.8]	227.3 [173.5, 409.5]	0.095
Creatinine (mg/dL) (median [IQR])	1.7 [1.4, 2.1]	2.0 [1.5, 2.5]	0.106
Troponin I (ng/mL) (median [IQR])	38.7 [16.6, 91.7]	48.2 [25.9, 107.9]	0.112
BUN (mg/dL) (median [IQR])	31.0 [23.4, 49.8]	41.9 [24.0, 66.0]	0.281
CRP (mg/L) (median [IQR])	15.0 [7.2, 33.8]	21.8 [6.6, 51.9]	0.467
BNP (pg/ml) (median [IQR])	338.2 [188.7, 957.1]	447.1 [198.8, 724.6]	0.808
Cystatin C (mg/L) (median [IQR])	1.9 [1.6, 2.4]	2.1 [1.3, 2.5]	0.974
Urinary biomarkers			
EGF (ug/g Cr) (median [IQR])	6.6 [2.3, 19.6]	14.2 [6.7, 31.9]	**0.049**
Creatinine (mg/dL) (median [IQR])	68.1 [35.1, 115.8]	44.6 [28.4, 84.8]	0.102
IGFBP-7 (ug/g Cr) (median [IQR])	27.5 [20.0, 43.4]	37.9 [25.7, 55.1]	0.141
Uromodulin (mg/g Cr) (median [IQR])	25.9 [14.7, 64.7]	39.0 [18.3, 84.4]	0.160
TIMP-2 (ug/g Cr) (median [IQR])	3.0 [1.9, 5.4]	3.8 [2.8, 5.8]	0.206
CCL-14 (ug/g Cr) (median [IQR])	1.6 [0.7, 3.3]	2.2 [1.4, 4.6]	0.208
KIM-1 (ug/g Cr) (median [IQR])	1.5 [0.6, 3.3]	0.8 [0.4, 3.1]	0.212
IGFBP-1 (ug/g Cr) (median [IQR])	21.0 [8.7, 36.3]	33.5 [13.3, 63.0]	0.23
FENa (median [IQR])	1.1 [0.3, 4.2]	2.7 [0.8, 4.8]	0.234
MCP-1 (ng/g Cr) (median [IQR])	225.8 [106.7, 467.1]	286.2 [141.2, 558.1]	0.362
ACR (mg/g Cr) (median [IQR])	69.8 [32.1, 217.3]	118.8 [58.3, 328.9]	0.363
LFABP-1 (ug/g Cr) (median [IQR])	5.3 [2.2, 9.5]	4.0 [2.5, 6.0]	0.469
NGAL (ug/g Cr) (median [IQR])	30.9 [19.2, 74.2]	38.8 [19.9, 75.1]	0.521
FEUrea (median [IQR])	28.0 [17.3, 42.6]	27.0 [16.5, 34.0]	0.55
AGT (ug/g Cr) (median [IQR])	4.7 [0.4, 40.1]	4.8 [0.5, 16.9]	0.764
A1M (mg/g Cr) (median [IQR])	63.7 [35.0, 103.7]	54.0 [28.7, 135.7]	0.773
TIMP-2*IGFBP-7 (ng/ml2/1000/g Cr) (median [IQR])	65.1 [32.2, 108.9]	68.6 [33.4, 124.4]	0.832
YKL-40 (ug/g Cr) (median [IQR])	1.3 [0.5, 3.9]	1.2 [0.8, 2.4]	0.837

ACR, Albumin to creatinine ratio; AGT, urinary angiotensinogen; A1M, alpha 1-microglobulin; BNP, brain natriuretic peptide; CCL-14, C-C motif chemokine ligand 14; Cr, creatinine; CRP, C-reactive protein; EGF, Epidermal Growth Factor; IQR, inter-quartile range; FENa, Fractional Excretion of Sodium; IGFBP-1, Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; KIM-1, Kidney injury molecule 1; L-FABP-1, liver-type fatty acid binding protein-1; MCP-1, monocyte chemotactic protein-1; NGAL, neutrophil gelatinase associated lipocalin; TIMP-2, tissue inhibitor of metalloproteinases-2; YKL-40, chitinase-3-like protein 1.

Table S5. Median, First and Third Quartile Values for Progressors versus Non-Progressors to the Secondary Outcome of Renal Replacement Therapy or Higher Stage of Worsening Renal Function Measured at Time of Worsening Renal Function in Acute Heart Failure Hospitalization

Variable	Non-progressor n=151	Progressor n=24	p-value
Serum/Plasma Biomarkers			
Galectin-3 (ng/ml) (median [IQR])	27.2 [20.9, 34.5]	39.4 [24.4, 63.7]	**0.011**
Creatinine (mg/dL) (median [IQR])	1.7 [1.4, 2.2]	2.0 [1.5, 2.5]	0.188
BUN (mg/dL) (median [IQR])	32.0 [23.4, 50.5]	41.4 [24.0, 66.0]	0.414
NGAL (ng/ml) (median [IQR])	194.0 [121.0, 358.8]	242.5 [158.8, 409.5]	0.215
BNP (pg/ml) (median [IQR])	346.9 [199.7, 946.1]	447.1 [159.8, 673.7]	0.69
Troponin I (ng/mL) (median [IQR])	40.5 [17.1, 100.8]	43.7 [25.3, 94.3]	0.76
Cystatin C (mg/L) (median [IQR])	1.9 [1.6, 2.5]	2.1 [1.7, 2.5]	0.977
CRP (mg/L) (median [IQR])	15.0 [6.9, 34.6]	21.8 [11.3, 40.7]	0.497
Urinary biomarkers			
EGF (ug/g Cr) (median [IQR])	6.6 [2.4, 18.3]	15.9 [7.0, 32.1]	**0.044**
NGAL (ug/g Cr) (median [IQR])	30.9 [19.1, 75.7]	40.4 [23.7, 55.6]	0.59
A1M (mg/g Cr) (median [IQR])	65.8 [35.0, 104.9]	45.8 [28.7, 90.5]	0.407
AGT (ug/g Cr) (median [IQR])	5.3 [0.5, 40.1]	3.4 [0.3, 16.9]	0.508
YKL-40 (ug/g Cr) (median [IQR])	1.3 [0.5, 3.9]	1.1 [0.8, 2.4]	0.985
IGFBP-1 (ug/g Cr) (median [IQR])	21.4 [8.7, 38.0]	33.5 [13.3, 50.4]	0.437
IGFBP-7 (ug/g Cr) (median [IQR])	27.8 [20.3, 43.8]	37.9 [21.4, 55.1]	0.319
TIMP-2*IGFBP-7 (ng/ml2/1000/g Cr) (median [IQR])	65.1 [32.2, 120.8]	68.6 [33.4, 111.9]	0.817
TIMP-2 (ug/g Cr) (median [IQR])	3.0 [2.0, 5.5]	3.8 [2.4, 5.5]	0.378
KIM-1 (ug/g Cr) (median [IQR])	1.5 [0.6, 3.5]	0.8 [0.4, 2.8]	0.192
LFABP-1 (ug/g Cr) (median [IQR])	5.3 [2.2, 9.5]	3.8 [2.1, 4.9]	0.25
MCP-1 (ng/g Cr) (median [IQR])	244.0 [107.8, 506.0]	158.7 [139.1, 542.4]	0.792
Uromodulin (mg/g Cr) (median [IQR])	27.3 [14.7, 67.4]	39.0 [18.3, 83.0]	0.322
CCL-14 (ug/g Cr) (median [IQR])	1.6 [0.7, 3.5]	1.9 [1.4, 3.4]	0.621
FENa (median [IQR])	1.2 [0.4, 4.1]	2.2 [0.8, 5.6]	0.343
FEUrea (median [IQR])	28.1 [18.0, 42.6]	22.2 [14.9, 34.0]	0.225
Creatinine (mg/dL) (median [IQR])	64.6 [31.9, 113.6]	44.9 [31.4, 84.8]	0.474
ACR (mg/g Cr) (median [IQR])	70.7 [32.1, 282.9]	118.8 [58.3, 259.4]	0.602

IQR, inter-quartile range; Abbreviations: NA, not applicable; BNP, brain natriuretic peptide; pNGAL, plasma neutrophil gelatinase associated lipocalin; sCr, serum creatinine; uNGAL, urinary neutrophil gelatinase associated lipocalin; A1M, alpha-1 microglobulin; L-FABP-1, liver-type fatty acid binding protein-1; KIM-1, kidney injury molecule-1; KIM-1, kidney injury molecule 1; AGT, urinary angiotensinogen; A1M, alpha 1-microglobulin; YKL-40, chitinase-3-like protein 1; MCP-1, monocyte chemotactic protein-1; TIMP-2, tissue inhibitor of metalloproteinases-2; IGFBP-1, Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; EGF, Epidermal Growth Factor; CCL-14, C-C motif chemokine ligand 14; FENa, Fractional Excretion of Sodium; FEUrea, Fractional Urea; ACR, Albumin to creatinine ratio; CRP, C-reactive protein
Biomarkers were compared using the Wilcoxon signed-rank test

Table S6. Odds of progression to a higher stage of worsening renal function or renal replacement therapy within 30 days in the highest tertile of biomarkers versus lowest tertile of biomarkers in unadjusted and adjusted logistic regression in individuals with stage 1 or 2 acute kidney injury in AKINESIS

Plasma Biomarkers (Tertile 3 versus Tertile 1)	**Unadjusted OR (95% CI)**	**p-value**	**Adjusted* OR (95% CI)**	**p-value**
Galectin-3	**3.5 (1.3-10.6)**	**0.018**	**3.5 (1.1-12.4)**	**0.041**
Urea	1.1 (0.4-3.0)	0.875	0.1 (0.0-0.9)	0.053
Cystatin C	1.9 (0.5-8.1)	0.337	4.7 (0.9-28)	0.076
Creatinine	2.5 (0.9-7.7)	0.099	2.3 (0.6-8.9)	0.223
NGAL	2.1 (0.7-6.5)	0.195	1.7 (0.5-6.2)	0.387
BNP	0.6 (0.2-1.7)	0.338	0.5 (0.2-1.5)	0.221
CRP	1.7 (0.5-7.2)	0.403	1.7 (0.5-6.9)	0.450
Troponin I	1.4 (0.5-4.6)	0.547	1.4 (0.5-4.6)	0.549
Urine Biomarkers (Tertile 3 versus Tertile 1)	Unadjusted OR (95% CI)	p-value	Adjusted* OR (95% CI)	p-value
EGF	3.7 (1-17.5)	0.065	3 (0.8-14.7)	0.126
A1M	0.6 (0.1-2)	0.400	0.3 (0.1-1.3)	0.122
LFABP-1	0.4 (0.1-1.8)	0.253	0.4 (0.0-1.8)	0.246
IGFBP-7	2.1 (0.7-7.4)	0.218	1.8 (0.5-6.5)	0.349
ACR	2.3 (0.6-11.7)	0.252	2 (0.5-10.3)	0.349
Creatinine	0.5 (0.2-1.7)	0.29	0.6 (0.2-1.9)	0.376
IGFBP-1	2.0 (0.6-7.0)	0.271	1.6 (0.5-6.1)	0.466
KIM-1	0.6 (0.2-2.0)	0.444	0.6 (0.2-2.2)	0.475
CCL-14	1.9 (0.4-9.9)	0.391	1.6 (0.4-8.6)	0.522
MCP-1	1.8 (0.5-7.4)	0.397	1.5 (0.4-6.4)	0.564
Uromodulin	1.8 (0.5-7.5)	0.360	1.5 (0.4-6.2)	0.567
AGT	0.7 (0.2-2.5)	0.552	0.7 (0.2-2.7)	0.609
TIMP-2	1.6 (0.5-5.8)	0.460	1.4 (0.4-5.1)	0.626
TIMP-2*IGFBP-7	1.2 (0.4-3.8)	0.765	1.2 (0.4-3.9)	0.780
uNGAL	1.1 (0.3-3.9)	0.823	0.9 (0.3-3.2)	0.879
YKL-40	0.7 (0.2-2.6)	0.603	0.9 (0.2-3.7)	0.923
Ratios (Tertile 3 versus Tertile 1)	Unadjusted OR (95% CI)	p-value	Adjusted* OR (95% CI)	p-value
FEUrea	0.5 (0.1-1.7)	0.264	0.6 (0.1-2.4)	0.450
FENa	1.5 (0.4-6.3)	0.554	1.2 (0.3-5.1)	0.828

*Adjusted for systolic blood pressure and BUN at the time of AKI diagnosis

A1M, alpha 1-microglobulin; AGT, angiotensinogen; BNP, brain natriuretic peptide; CCL-14, chemokine ligand 14; CI, confidence interval; CRP, C-reactive protein; EGF, epidermal growth factor; FeNa, fractional excretion of sodium; FeUrea, fractional excretion of urea; IGFBP-1, Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; L-FABP-1, KIM-1, kidney injury molecule-1; LFABP-1, liver-type fatty acid–binding protein-1; MCP-1, monocyte chemotactic protein-1; NGAL, neutrophil gelatinase–associated lipocalin; OR, odds ratio; TIMP-2, tissue inhibitor of metalloproteinases-2; YKL-40, chitinase-3-like protein 1

Table S7. Category-free net reclassification index and integrated discrimination index for the prediction of progression from Stage 1-2 WRF within 72 hours of hospital admission to higher WRF stage, RRT or death within 30 days.

Biomarker	cfNRI (95% CI)	P	$cfNRI_{ev}$ (95% CI)	P_{ev}	$cfNRI_{ne}$ (95% CI)	P_{ne}	IDI (95% CI)	P_{IDI}
Galectin-3	0.52 (0.14-0.89)	**0.007**	0.19 (-0.15-0.53)	0.28	0.33 (0.17-0.48)	**<0.001**	0.1 (0.04-0.16)	**0.002**
Troponin I	0.21 (-0.17-0.59)	0.278	-0.06 (-0.41-0.28)	0.723	0.27 (0.12-0.43)	**<0.001**	0.02 (0-0.04)	0.108
TIMP-2	0.28 (-0.18-0.75)	0.227	0.05 (-0.38-0.47)	0.827	0.24 (0.06-0.41)	**0.008**	0.02 (-0.01-0.05)	0.21
CCL-14	0.05 (-0.41-0.52)	0.819	-0.05 (-0.47-0.38)	0.827	0.1 (-0.08-0.28)	0.267	0.01 (0-0.03)	0.165
uCreatinine	0.46 (0.08-0.83)	**0.016**	0.33 (0-0.67)	0.053	0.12 (-0.04-0.29)	0.131	0.01 (0-0.02)	0.255
Uromodulin	0.22 (-0.25-0.68)	0.358	0.05 (-0.38-0.47)	0.827	0.17 (-0.01-0.35)	0.062	0.01 (-0.02-0.04)	0.36
IGFBP-7	0.25 (-0.21-0.71)	0.287	0.05 (-0.38-0.47)	0.827	0.2 (0.03-0.38)	**0.024**	0.01 (-0.01-0.04)	0.337
IGFBP-1	0.13 (-0.33-0.6)	0.576	0.05 (-0.38-0.47)	0.827	0.08 (-0.1-0.26)	0.356	0.01 (-0.01-0.03)	0.288
EGF	0.28 (-0.18-0.74)	0.235	0.14 (-0.28-0.57)	0.508	0.14 (-0.04-0.31)	0.137	0.01 (-0.01-0.03)	0.413
TIMP-2* IGFBP-7	0.03 (-0.43-0.49)	0.897	0.05 (-0.38-0.47)	0.827	-0.02 (-0.2-0.16)	0.854	0.01 (-0.01-0.02)	0.322
MCP-1	0.02 (-0.44-0.48)	0.932	-0.05 (-0.47-0.38)	0.827	0.07 (-0.11-0.25)	0.46	0.01 (-0.01-0.02)	0.437
CRP	0.21 (-0.26-0.68)	0.382	0.2 (-0.23-0.63)	0.361	0.01 (-0.18-0.2)	0.923	0 (0-0.01)	0.719
BNP	0.08 (-0.31-0.46)	0.694	0 (-0.35-0.35)	1	0.08 (-0.09-0.24)	0.356	0 (0-0)	0.853
uNGAL	0.02 (-0.38-0.41)	0.934	-0.07 (-0.42-0.29)	0.714	0.08 (-0.08-0.25)	0.316	0 (0-0)	0.703
AGT	0.05 (-0.42-0.51)	0.841	0.05 (-0.38-0.47)	0.827	0 (-0.18-0.18)	1	0 (0-0)	0.892
LFABP-1	0.39 (-0.03-0.82)	0.07	0.43 (0.04-0.82)	**0.03**	-0.03 (-0.21-0.15)	0.713	0 (0-0)	0.998
FEUrea	0.19 (-0.28-0.66)	0.429	0.26 (-0.17-0.7)	0.234	-0.07 (-0.26-0.11)	0.444	0 (0-0)	0.897
ACR	0.27 (-0.21-0.75)	0.277	0.16 (-0.29-0.6)	0.486	0.11 (-0.08-0.29)	0.25	0 (0-0)	0.753
Cystatin C	0.28 (-0.18-0.75)	0.235	0.2 (-0.23-0.63)	0.361	0.08 (-0.1-0.27)	0.383	0 (0-0)	0.771
YKL-40	0.01 (-0.45-0.47)	0.967	-0.14 (-0.57-0.28)	0.508	0.15 (-0.03-0.33)	0.094	0 (-0.01-0.02)	0.622
KIM-1	0.31 (-0.15-0.77)	0.182	0.14 (-0.28-0.57)	0.508	0.17 (-0.01-0.35)	0.062	0 (-0.01-0.02)	0.741
A1M	0.42 (-0.02-0.86)	0.063	0.33 (-0.07-0.74)	0.105	0.08 (-0.1-0.26)	0.356	0 (-0.01-0.01)	0.358
FENa	0.25 (-0.23-0.73)	0.311	0.16 (-0.29-0.6)	0.486	0.09 (-0.1-0.28)	0.338	0 (-0.01-0.01)	0.734
pNGAL	0.16 (-0.22-0.54)	0.41	0.12 (-0.22-0.47)	0.476	0.03 (-0.13-0.2)	0.676	0 (-0.01-0)	0.857

P, P-Value; cfNRI, category-free NRI; $cfNRI_{ev}$, cfNRI for events; $cfNRI_{ne}$, cfNRI for non-events; IDI, Integrated Discrimination Improvement; Abbreviations: NA, not applicable; BNP, brain natriuretic peptide; uCr, urinary creatinine; pNGAL, plasma neutrophil gelatinase associated lipocalin; uNGAL, urinary neutrophil gelatinase associated lipocalin; L-FABP-1, liver-type fatty acid binding protein-1; KIM-1, kidney injury molecule-1; KIM-1, kidney injury molecule 1; uAGT, urinary angiotensinogen; A1M, alpha 1-microglobulin; YKL-40, chitinase-3-like protein 1; MCP-1, monocyte chemotactic protein-1; TIMP-2, tissue inhibitor of metalloproteinases-2; IGFBP-1, Insulin-like growth factor-binding protein 1; IGFBP-7, Insulin-like growth factor-binding protein 7; ACR, Albumin to creatinine ratio; uNa, urinary Sodium; urUrea, urinary Urea; pCysC, plasma Cystatin C; CRP, C-reactive protein; FENa, Fractional Excretion of Sodium; EGF, Epidermal Growth Factor; CCL-14, C-C motif chemokine ligand 14