SUPPLEMENTARY APPENDIX

Table S1. Site of Infection and Risk of Developing AKD

Site of Infection	Odds Ratio for Developing AKD	95% CI	P value
Pneumonia	0.66	0.43-1.02	0.063
Urosepsis	1.60	1.04-2.44	0.031
Intra-abdominal	0.83	0.46-1.49	0.527
Skin and soft-tissue	1.04	0.49-2.21	0.925
Catheter-related	1.33	0.37-4.76	0.739
Central nervous system	1.99	0.28-14.24	0.605
Endocarditis	1.99	0.28-14.24	0.605
Unknown	0.81	0.46-1.44	0.475

Table S2. TIMP-2*IGFBP7 Level Changes Between Two Time Points and Predictive Value for AKD at 7 days

Time Period	Level Change, median (interquartile range)		*P* Value	AUC-ROC for Predicting AKD	95% CI	*P* Value
	AKD	Early Reversal				
0 to 6 hours	0.12 (-0.67-2.10) N = 94	0.30 (-0.10-1.64) N = 226	0.24	0.54	0.47-0.62	0.28
6 to 24 hours	0.25 (-0.08-1.13) N = 110	0.07 (-0.14-0.70) N = 240	0.07	0.56	0.50-0.63	0.07
0 to 24 hours	0.23 (-0.49-2.38) N = 96	0.36 (-0.03-2.30) N = 215	0.16	0.55	0.48-0.62	0.19

AKD, acute kidney disease; AUC-ROC, area under the receiver operating characteristic curve; CI, confidence interval.

The level change was calculated by subtracting the later value from the early one.

Table S3. Clinical Models with Urinary Biomarkers for Predicting AKD

Variable	Clinical Model with Biomarker(s) at 6 h Odds Ratio (95% CI)		
	TIMP-2*IGFBP7 (N = 386)	**NGAL (N = 125)**	**TIMP-2*IGFBP7 and NGAL (N = 124)**
Age, by 5 years	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
Male	2.53 (1.33-4.82)	3.06 (1.16-8.05)	3.09 (1.24-7.69)
Race			
• African American vs White	1.93 (0.99-3.75)	1.41 (0.56-3.52)	1.33 (0.57-3.13)
• Others vs White	1.01 (0.32-3.19)	-	-
Hypertension	0.76 (0.50-1.14)	1.79 (0.61-5.37)	1.72 (0.52-5.64)
Cardiac disease	1.06 (0.44-2.53)	0.22 (0.03-1.77)	0.20 (0.04-0.98)
APS-III score,‡ by units of 10	1.17 (1.04-1.31)	1.04 (0.78-1.39)	1.05 (0.84-1.31)
Weight-adjusted urine output,†‡ by 100 mL	0.99 (0.98-1.01)	0.99 (0.97-1.02)	0.99 (0.96-1.02)
Vasopressor*	1.25 (0.64-2.43)	0.79 (0.19-3.33)	0.81 (0.20-3.39)
Mechanical ventilation*	0.45 (0.21-0.93)	0.71 (0.11-4.56)	0.73 (0.15-3.65)
Biomarker(s) at 6 h	1.27 (1.07-1.49)	1.04 (1.01-1.08)	0.90 (0.60-1.36) for TIMP-2*IGFBP7;§ 1.05 (1.01-1.09) for NGAL‡
AUC-ROC (95% CI)	0.72 (0.66-0.77)	0.74 (0.65-0.83)	0.74 (0.65-0.83)
Goodness-of-Fit *P* value	0.76	0.57	0.25
P value for comparison of AUC-ROC with clinical model alone	0.18	0.02	0.02

AUC-ROC, area under the receiver operating characteristic curve; CI, confidence interval; IGFBP7, insulin-like growth factor-binding protein 7; NGAL, neutrophil gelatinase-associated lipocalin; TIMP-2, tissue inhibitor of metalloproteinases-2.

‡Square root tranformation was used for selected variables in the model.

§Log tranformation was used for selected variable in the model.

Table S4. Validation of Clinical Model for Predicting Non-Recovery AKI at Hospital Discharge

Variable	OR	95% CI	*P* value
Age, by 5 years	1.00	1.00-1.00	0.45
Male	1.69	1.19-2.40	0.003
Race			
• African American vs White	1.45	0.97-2.14	0.07
• Others vs White	1.86	0.87-4.02	0.11
Hypertension	0.69	0.48-1.01	0.05
Cardiac disease	0.85	0.49-1.47	0.56
APS-III score,‡ by units of 10	1.11	1.04-1.19	0.002
Weight-adjusted urine output,†‡ by 100 mL	0.98	0.97-0.99	<0.001
Vasopressor*	1.13	0.71-1.79	0.60
Mechanical ventilation*	1.05	0.66-1.69	0.83

APS-III, Acute Physiology and Chronic Health Evaluation III; CI, confidence interval; OR, odds ratio.

N = 584; area under the receiver operating characteristic curve = 0.68 (95% CI, 0.64-0.73); Goodness-of-Fit *P* value = 0.45.

*Captured in 6 hours after ICU admission.

†The available urine volume in the 24 hours after ICU admission was summed and divided by the weight.

‡Square root tranformation was used for selected variables in the model.

Table S5. Urinary Biomarkers for Predicting Non-Recovery AKI at Hospital Discharge

Urinary Biomarker	Time Measured (hours)	N	AUC-ROC for Prediction of Non-Recovery AKI	95% CI	*P* value
TIMP-2*IGFBP7	0	425	0.54	0.48-0.59	0.19
	6	468	0.62	0.56-0.66	<0.001
	24	455	0.62	0.56-0.67	<0.001
NGAL	0	65	0.52	0.38-0.67	0.75
	6	150	0.59	0.50-0.69	0.046
	24	150	0.57	0.48-0.66	0.13
KIM-1	0	206	0.56	0.48-0.64	0.16
	6	223	0.55	0.48-0.63	0.17
	24	214	0.53	0.45-0.60	0.52
L-FABP	0	104	0.53	0.42-0.65	0.55
	6	106	0.57	0.46-0.68	0.23
	24	105	0.55	0.44-0.67	0.36
Type IV collagen	0	193	0.56	0.48-0.65	0.13
	6	210	0.60	0.52-0.68	0.01
	24	201	0.55	0.47-0.63	0.25

AKI, acute kidney injury; AUC-ROC, area under the receiver operating characteristic curve; CI, confidence interval; IGFBP7, insulin-like growth factor-binding protein 7; KIM-1, kidney injury molecule-1; L-FABP, liver-type fatty acid binding protein; NGAL, neutrophil gelatinase-associated lipocalin; TIMP-2, tissue inhibitor of metalloproteinases-2.

Table S6. Clinical Model with Urinary Biomarkers for Predicting Non-Recovery AKI at Hospital Discharge

Variable	Clinical Model with Biomarker(s) Odds Ratio (95% CI)					
	TIMP-2*IGFBP7 (6 h)[§] (N = 465)	**TIMP-2*IGFBP7 (24 h)[§] (N = 454)**	**NGAL (6 h)[‡] (N = 150)**	**Type IV Collagen (6 h)[§] (N = 208)**	**TIMP-2*IGFBP7 (6 h)[§] and NGAL (6 h)[‡] (N = 149)**	**TIMP-2*IGFBP7 (6 h)[§] and Type IV Collagen (6 h)[§] (N = 199)**
Age, by 5 years	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
Male	1.81 (1.22-2.71)	1.69 (1.13-2.52)	1.69 (0.83-3.44)	2.37 (1.22-4.63)	1.72 (0.83-3.55)	2.40 (1.17-4.88)
Race						
• African American vs White	1.42 (0.92-2.22)	1.52 (0.98-2.34)	0.96 (0.46-2.00)	1.14 (0.57-2.28)	0.92 (0.44-1.93)	1.02 (0.49-2.09)
• Others vs White	1.55 (0.68-3.56)	1.63 (0.68-3.89)	0.44 (0.04-5.12)	0.80 (0.26-2.45)	0.41 (0.04-4.77)	0.72 (0.23-2.26)
Hypertension	0.89 (0.58-1.35)	0.77 (0.51-1.18)	1.15 (0.52-2.53)	1.62 (0.83-3.17)	1.08 (0.49-2.40)	1.71 (0.85-3.41)
Cardiac disease	1.04 (0.57-1.92)	1.06 (0.58-1.94)	0.38 (0.12-1.26)	0.60 (0.20-1.76)	0.35 (0.10-1.20)	0.47 (0.15-1.49)
APS-III score,[‡] by units of 10	1.08 (1.00-1.12)	1.09 (1.00-1.18)	0.97 (0.83-1.14)	1.15 (1.00-1.32)	0.98 (0.84-1.16)	1.16 (1.00-1.34)
Weight-adjusted urine output,[†‡] by 100 mL	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.00 (0.98-1.02)	0.99 (0.98-1.01)	1.00 (0.98-1.02)	0.99 (0.97-1.01)
Vasopressor*	1.09 (0.66-1.80)	1.29 (0.76-2.18)	0.65 (0.26-1.65)	1.53 (0.69-3.38)	0.68 (0.27-1.73)	1.66 (0.72-3.79)
Mechanical ventilation*	1.33 (0.77-2.29)	0.96 (0.55-1.67)	2.30 (0.76-6.86)	1.09 (0.46-2.59)	2.31 (0.77-6.95)	1.05 (0.43-2.55)
Biomarker(s) at 6 h	1.16 (1.00-1.33)	1.23 (1.04-1.45)	1.02 (1.00-1.05)	1.27 (0.99-1.64)	0.91 (0.67-1.22) for TIMP-2*IGFBP7; 1.02 (1.00-1.06) for NGAL	1.06 (0.80-1.40) for TIMP-2*IGFBP7; 1.30 (0.96-1.75) for type IV collagen
AUC-ROC (95% CI)	0.68 (0.63-0.73)	0.67 (0.62-0.72)	0.66 (0.57-0.75)	0.71 (0.64-0.78)	0.66 (0.57-0.75)	0.72 (0.65-0.79)
Goodness-of-Fit *P* value	0.67	0.21	0.23	0.57	0.76	0.47
P value for comparison of AUC-ROC with clinical model alone	0.14	0.25	0.07	0.09	0.09	0.07

AUC-ROC, area under the receiver operating characteristic curve; CI, confidence interval; IGFBP7, insulin-like growth factor-binding protein 7; NGAL, neutrophil gelatinase-associated lipocalin; TIMP-2, tissue inhibitor of metalloproteinases-2.

[‡]Square root tranformation was used for selected variables and biomarker in the model.

[§]Log tranformation was used for selected biomarker(s) in the model.

Modified STROBE Statement—checklist of items that should be included in reports of observational studies (Cohort/Cross-sectional and case-control studies)

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	12
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	13
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	12
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement).	13-14
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at (if applicable)	5, Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14-15
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	14-15
		(*b*) Describe any methods used to examine subgroups and interactions	14-15
		(*c*) Explain how missing data were addressed	14
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	-
		(*e*) Describe any sensitivity analyses	8-9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	5

		confirmed eligible, included in the study, completing follow-up, and analyzed	
		(c) **Use of a flow diagram**	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5-6, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 3
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	6-8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6-8
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.