

Supplemental Data List of Figures

Supplemental Data Figure S1 A and B

NGAL concentrations from both cohorts for patients with and without sCr/UO-based AKI .

Supplemental Data Figure S2 A-D

A) AUC-ROC for v sCr/UO-based AKI according to the RIFLE criteria (N=14) in the Magdeburg cohort, N100; AUC = 0.757 (0.600 – 0.914), SE 0.08, $P = 0.001$.

B) AUC-ROC for for NGAL predicting sCr/UO-based AKI according to the KDIGO criteria (N=23) in the Magdeburg cohort, N100; AUC = 0.650 (0.511 – 0.789), SE 0.071, $P = 0.034$.

C) AUC-ROC for for NGAL predicting sCr/UO-based AKI according to the RIFLE criteria (N=24) in the Berlin cohort, N199; AUC = 0.724 (0.612 – 0.836), SE 0.057, $P < 0.001$.

D) AUC-ROC for for NGAL predicting sCr/UO-based AKI according to the KDIGO criteria (N=59) in the Berlin cohort, N199; AUC = 0.632 (0.543 – 0.720), SE 0.045, $P = 0.003$.

Supplemental Data Figure S3

Proportion of patients with renal impairment additionally identified by urinary NGAL only in relation to the proportion of patients with AKI based on conventional RIFLE/KDIGO criteria

Supplemental Data Figure S4

Proportion of patients with renal impairment additionally identified by urinary NGAL only and not by RIFLE/KDIGO criteria (subclinical AKI, subfunctional AKI, AKI stage 1S) in relation to the proportion of patients diagnosed to have any renal impairment

Supplemental Data Figure S5 A-D

Assessment of the magnitude of risk-disparity between the methodologies of cutoff value-selection and the RIFLE or KDIGO AKI classification

Supplemental Data Tables

Supplemental Data Table S1 A and B

A) Perioperative Characteristics of 100 patients in the Magdeburg Cohort with complete serum creatinine and urinary NGAL data

B) Perioperative characteristics of 199 patients in the Berlin cohort with complete serum creatinine and urinary NGAL data

Supplemental Data Table 1 A: Perioperative Characteristics of 100 patients in the Magdeburg Cohort with complete serum creatinine and urinary NGAL data

Variable	No RIFLE AKI N=86 (86.0%)	RIFLE AKI N=14 (14.0%)	P*	No KDIGO AKI N=77 (77.0%)	KDIGO AKI N=23 (23.0%)	P**
Age, yrs	71 (62 – 75)	70 (60 – 77)	0.838	71 (62 – 75)	70 (62 – 76)	0.631
Sex, female, N (%)	25 (29.1)	4 (28.6)	1.000	22 (28.6)	7 (30.4)	0.863
Diabetes mellitus, oral antidiabetics, N (%)	23 (26.7)	5 (35.7)	0.527	18 (23.4)	10 (43.5)	0.060
Insulin-dependent diabetes mellitus, N (%)	12 (14.0)	5 (35.7)	0.059	12 (15.6)	5 (21.7)	0.532
Arterial hypertension, N (%)	84 (97.7)	13 (92.9)	0.367	75 (97.4)	22 (95.7)	0.548
Left ventricular dysfunction, N (%)‡	40 (46.5)	10 (71.4)	0.084	35 (45.5)	15 (65.2)	0.096
Hypercholesterolemia, N (%)	41 (47.7)	5 (38.5)	0.535	36 (46.8)	10 (45.5)	0.914
<i>Kidney functional and kidney biomarker values</i>						
Preoperative serum creatinine, µmol/L	83 (72 – 102)	130 (85 – 175)	0.004	83 (72 – 100)	107 (88 – 146)	<0.001
Preoperative eGFR mL/min/1.73m ²	75.9 (60.8 – 90.0)	45.3 (32.4 – 73.6)	0.004	77.5 (61.1 – 91.0)	54.5 (33.8 – 73.2)	<0.001
Urine NGAL concentration (ng/mL) at ICU admission	6.5 (3.0 – 12.5)	34.6 (6.6 – 191.3)	0.002	6.7 (3.1 – 12.6)	11.8 (5.0 – 72.0)	0.029
<i>Procedures</i>			0.154			0.373
CABG surgery, N (%)	41 (47.7)	7 (50.0)		39 (50.6)	9 (39.1)	
Valvular surgery, N (%)	27 (31.4)	2 (14.3)		22 (28.6)	7 (30.4)	
CABG and valvular surgery, N (%)	15 (17.4)	4 (28.6)		14 (28.2)	5 (21.7)	
Thoracic aortic surgery, N (%)	0 (0.0)	1 (7.1)		0 (0.0)	1 (4.3)	
Valvular and aortic surgery, N (%)	3 (3.5)	0 (0.0)		2 (2.6)	1 (4.3)	
Redo cardiac surgery, N (%)	3 (3.5)	0 (0.0)	1.000	2 (2.6)	1 (4.3)	0.548
Cardiopulmonary bypass time, min.	83 (61 – 108)	95 (75 – 120)	0.136	81 (61 – 106)	95 (73 – 128)	0.075
<i>Adverse Outcome</i>						
Postoperative kidney replacement therapy (KRT), N (%)	0 (0.0)	6 (42.9)	<0.001	0 (0.0)	6 (26.1)	<0.001
In-hospital mortality, N (%)	0 (0.0)	3 (21.4)	0.002	0 (0.0)	3 (13.0)	0.011
Combined KRT or In-hospital mortality	0 (0.0)	6 (42.9)	<0.001	0 (0.0)	6 (26.1)	<0.001

Numbers denote median (25.-75. percentile) or frequency (%) where appropriate. AKI, acute kidney injury; CABG, coronary artery bypass graft;

NGAL, urine neutrophil gelatinase associated lipocalin, RIFLE, risk injury failure end-stage renal disease classification

KDIGO, Kidney Disease Improving Global Outcome classification of AKI

* P value for RIFLE-AKI vs. No-RIFLE-AKI; ** P-value refers to comparison of patients with KDIGO-AKI vs. No-KDIGO-AKI,

‡ congestive heart failure defined as NYHA class 3 or 4 or Left ventricular ejection fraction (LVEF) <35%.

eGFR, estimated glomerular filtration rate calculated using the Chronic Kidney Disease Epidemiology Collaboration

(CKD-EPI) formula; ICU, intensive care unit; KRT, kidney replacement therapy; yrs, years

Supplemental Data Table 1 B: Perioperative characteristics of 199 patients in the Berlin cohort with complete serum creatinine and urinary NGAL data

Variable	No RIFLE AKI N=175 (87.9%)	RIFLE AKI N=24 (12.1%)	P*	No KDIGO AKI N=140 (70.4%)	KDIGO AKI N=59 (29.6%)	P**
Age, yrs	68 (59 – 74)	73 (68 – 77)	0.016	68 (58 – 74)	71 (65 – 77)	0.009
Sex, female, N (%)	51 (29.1)	8 (33.3)	0.673	44 (31.4)	15 (25.4)	0.397
Non insulin-dependent diabetes mellitus, N (%)	34 (19.4)	5 (20.8)	0.527	27 (19.3)	12 (20.3)	0.864
Insulin-dependent diabetes mellitus, N (%)	9 (5.1)	0 (0.0)	0.603	6 (4.3)	3 (5.1)	0.726
Arterial hypertension, N (%)	130 (74.3)	23 (95.8)	0.019	103 (73.6)	50 (84.7)	0.088
Left ventricular dysfunction, N (%)‡	34 (19.4)	7 (29.2)	0.285	24 (17.1)	17 (28.8)	0.063
Hypercholesterolemia, N (%)	113 (64.6)	17 (70.8)	0.546	87 (62.1)	43 (72.9)	0.146
<i>Kidney functional and kidney biomarker values</i>						
Preoperative serum creatinine, µmol/L	88 (78 – 106)	97 (85 – 124)	0.077	85 (75 – 97)	106 (88 – 124)	<0.001
Preoperative eGFR mL/min/1.73m ²	71.7 (56.6 – 87.0)	57.1 (45.2 – 77.7)	0.015	76.4 (59.2 – 88.2)	57.1 (45.8 – 77.9)	<0.001
Urine NGAL concentration (ng/mL) at ICU admission	8.1 (1.5 – 40.3)	125.3 (9.6 – 421.9)	<0.001	7.7 (1.4 – 29.3)	39.0 (4.5 – 206.4)	0.003
<i>Procedures</i>						
CABG surgery, N (%)	32 (18.3)	4 (16.7)	1.000	24 (17.1)	12 (20.3)	0.593
Valvular surgery, N (%)	77 (44.0)	12 (50.0)	0.579	64 (45.7)	25 (42.4)	0.665
CABG and valvular surgery, N (%)	48 (27.4)	6 (25.0)	0.802	40 (28.6)	14 (23.7)	0.483
Valvular and aortic surgery, N (%)	17 (9.7)	1 (4.2)	0.703	12 (8.6)	6 (10.2)	0.720
Redo cardiac surgery, N (%)	42 (24.0)	10 (41.7)	0.065	32 (22.9)	20 (33.9)	0.105
Cardiopulmonary bypass time, min.	120 (92 – 148)	168 (120 – 277)	<0.001	119 (153 – 144)	140 (94 – 189)	0.007
<i>Adverse Outcome</i>						
Postoperative kidney replacement therapy (KRT), N (%)	5 (2.9)	8 (33.3)	<0.001	0 (0.0)	13 (22.0)	<0.001
In-hospital mortality, N (%)	5 (2.9)	8 (33.3)	<0.001	3 (2.1)	10 (16.9)	<0.001
Combined KRT or In-hospital mortality	8 (4.6)	13 (54.2)	<0.001	3 (2.1)	18 (30.5)	<0.001

Numbers denote median (25.-75. percentile) or frequency (%) where appropriate. AKI, acute kidney injury; CABG, coronary artery bypass graft;

NGAL, urine neutrophil gelatinase associated lipocalin, RIFLE, risk injury failure end-stage renal disease classification

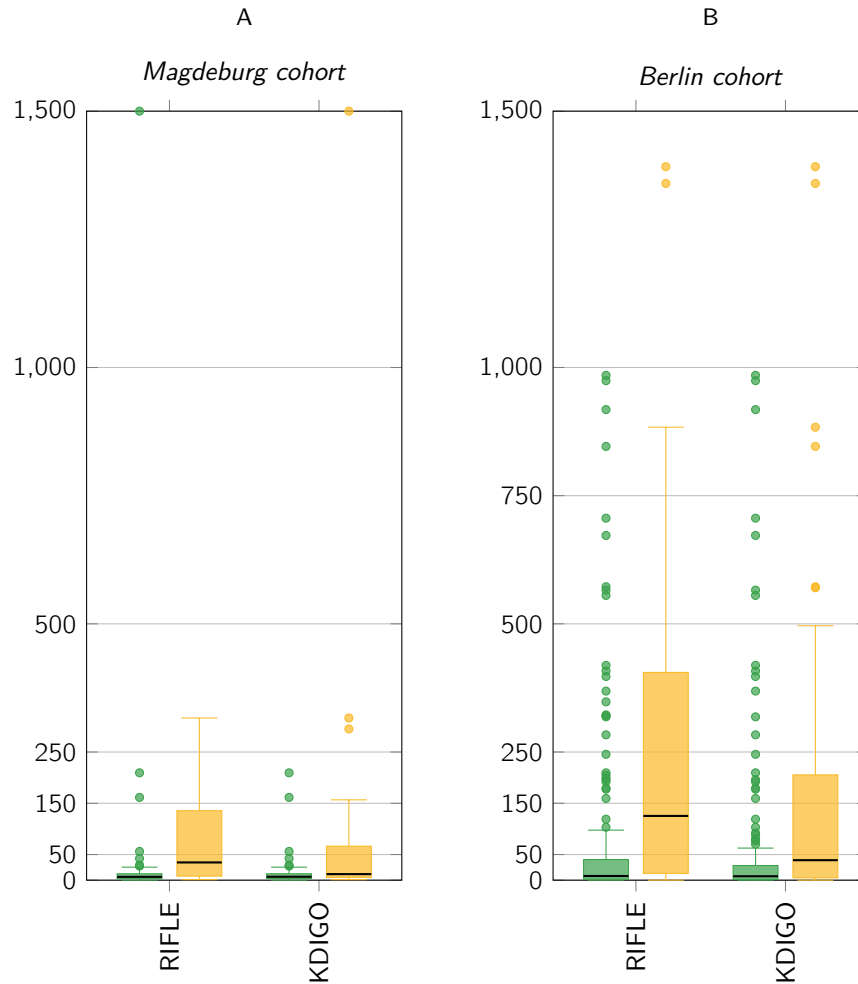
KDIGO, Kidney Disease Improving Global Outcome classification of AKI

* P value for RIFLE-AKI vs. No-RIFLE-AKI; ** P-value refers to comparison of patients with KDIGO-AKI vs. No-KDIGO-AKI,

‡ congestive heart failure defined as NYHA class 3 or 4 or Left ventricular ejection fraction (LVEF) <35%.

eGFR, estimated glomerular filtration rate calculated using the Chronic Kidney Disease Epidemiology Collaboration

(CKD-EPI) formula; ICU, intensive care unit; KRT, kidney replacement therapy; yrs, years



Supplemental Data Figure 1: Box and whiskers plots representing range of urinary neutrophil gelatinase-associated lipocalin (NGAL) concentrations for patients without AKI ■ and with SCr/UO-based AKI ■

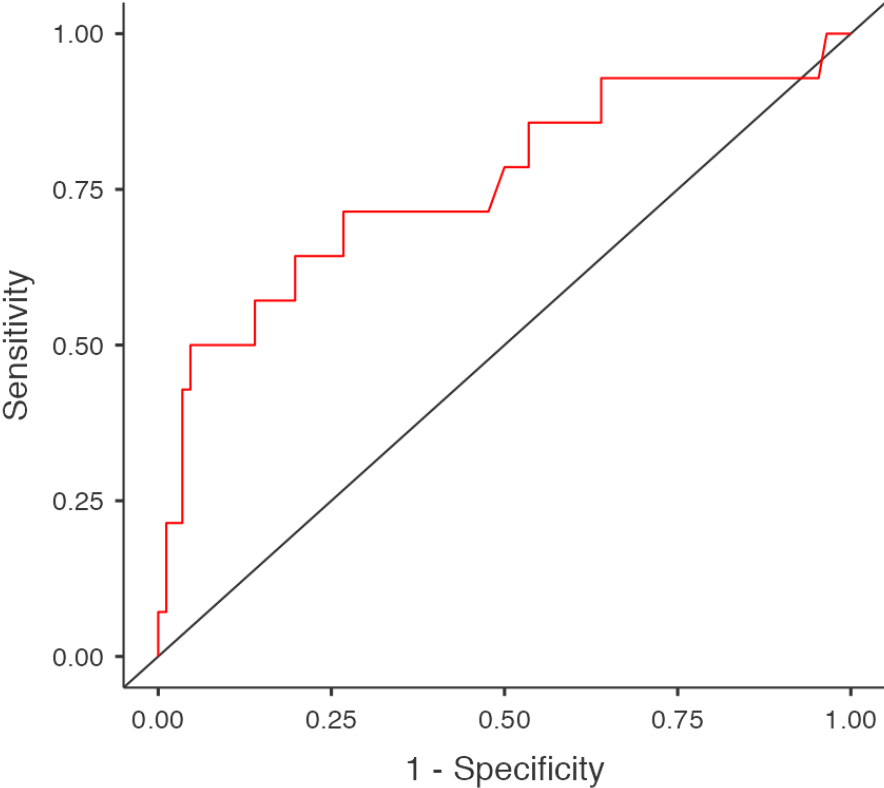
according to RIFLE and KDIGO in the Magdeburg and Berlin study cohorts. In both cohorts, there is a number of patients with elevated NGAL-values not meeting SCr/UO-based AKI criteria (potential subfunctional AKI, AKI 1 S).

Boxes represent median (25th - 75th IQR, interquartile range), whiskers represent $\pm 1.5 \times IQR$, ● represent outliers; extreme outliers (>1500 ng/mL) are hidden to improve scale interpretation and comparability of AKI vs. AKI-free patients.

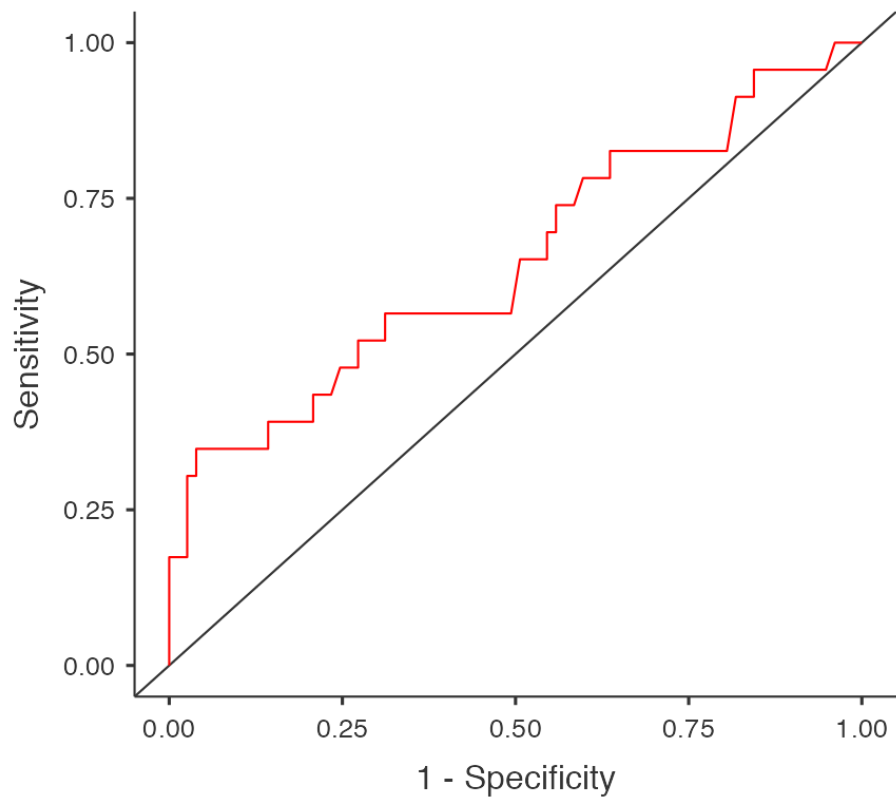
Abbreviations: AKI, acute kidney injury; RIFLE, Risk, injury, failure, loss, end-stage classification of AKI; KDIGO, Kidney disease improving global outcome classification of AKI.

Supplemental Data Figure 2

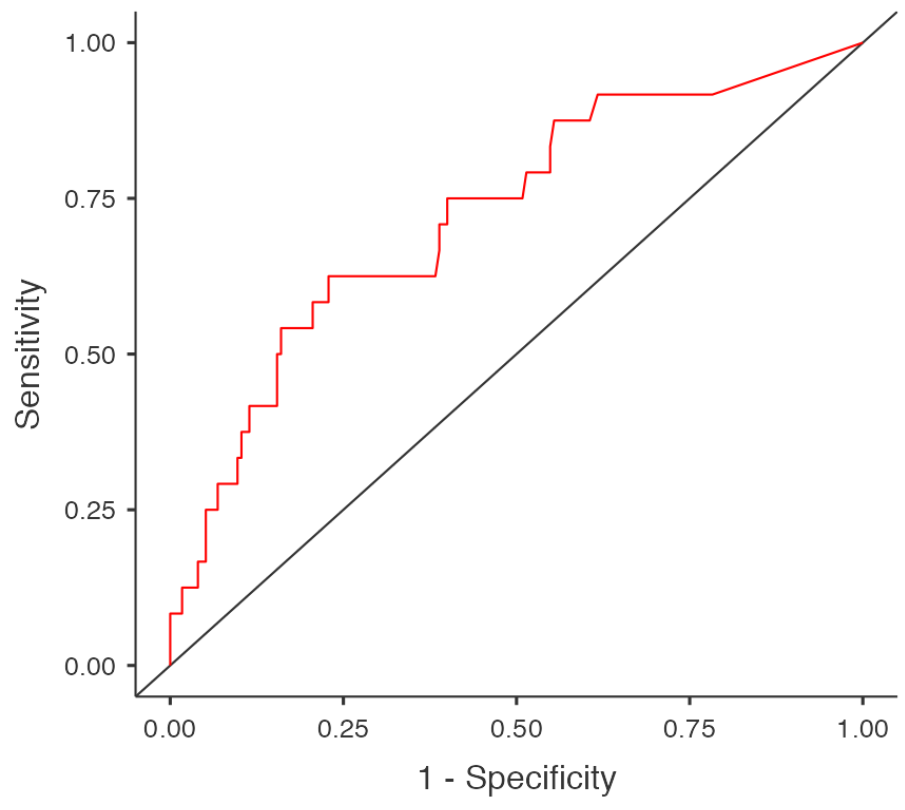
A



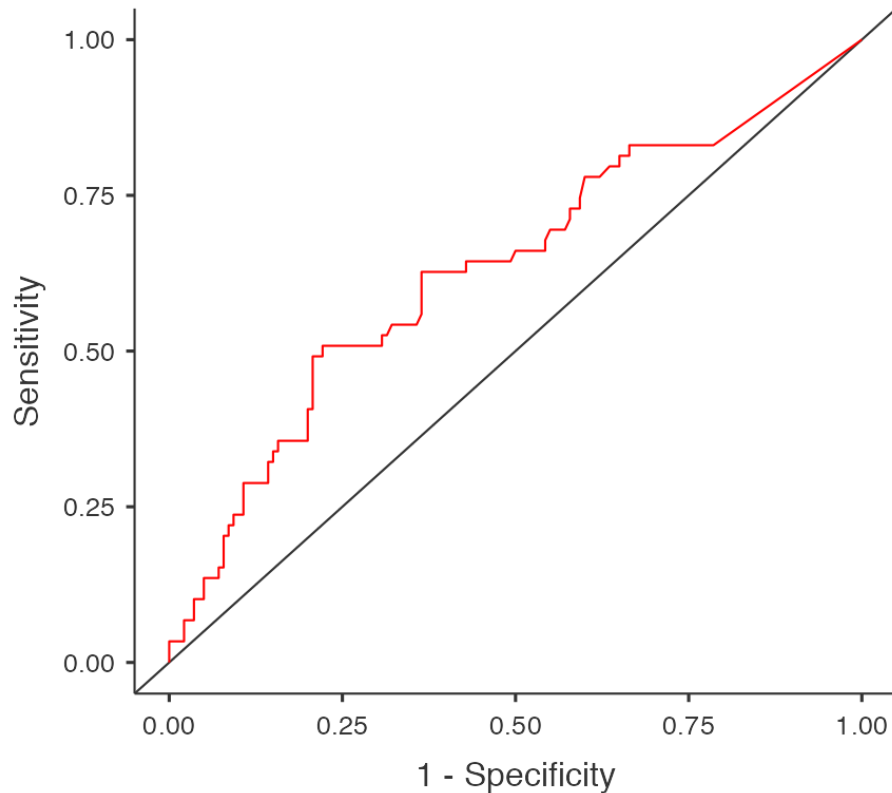
B



c



D



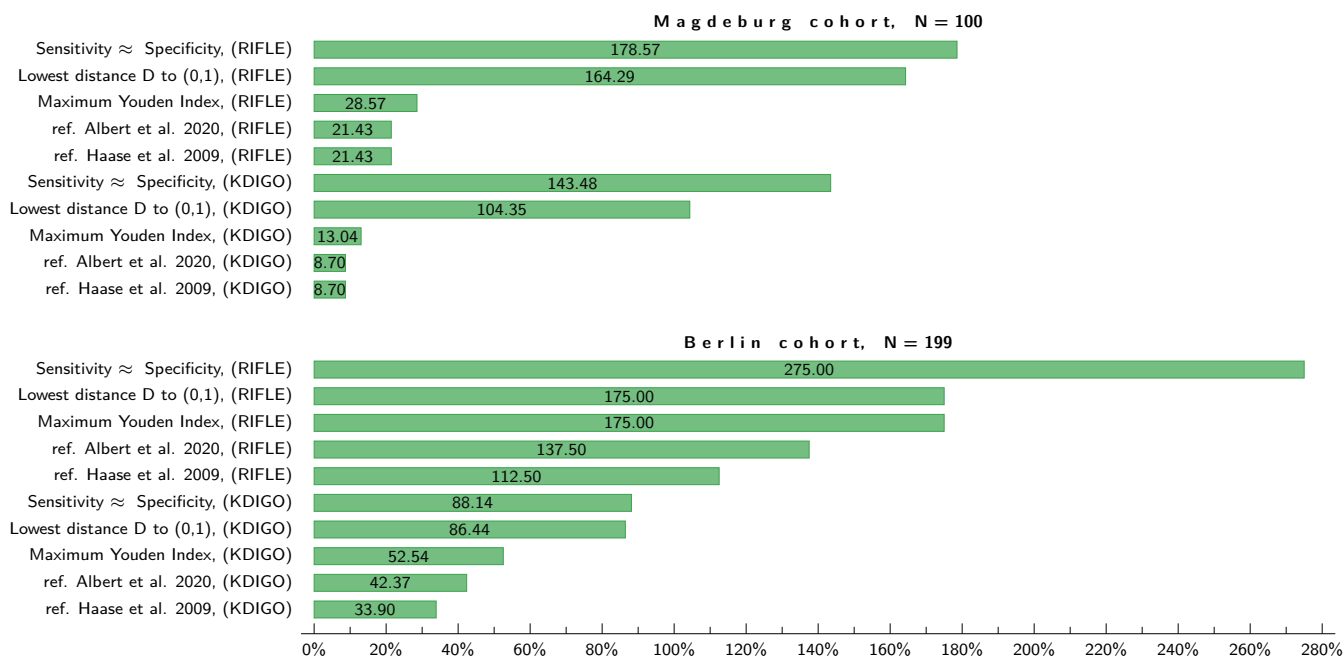
Supplemental Data Figure 2 A-D:

A) AUC-ROC for v SCr/UO-based AKI according to the RIFLE criteria (N=14) in the Magdeburg cohort, N100; AUC = 0.757 (0.600 – 0.914), SE 0.08, $P = 0.001$.

B) AUC-ROC for for NGAL predicting SCr/UO-based AKI according to the KDIGO criteria (N=23) in the Magdeburg cohort, N100; AUC = 0.650 (0.511 – 0.789), SE 0.071, $P = 0.034$.

C) AUC-ROC for for NGAL predicting SCr/UO-based AKI according to the RIFLE criteria (N=24) in the Berlin cohort, N199; AUC = 0.724 (0.612 – 0.836), SE 0.057, $P < 0.001$.

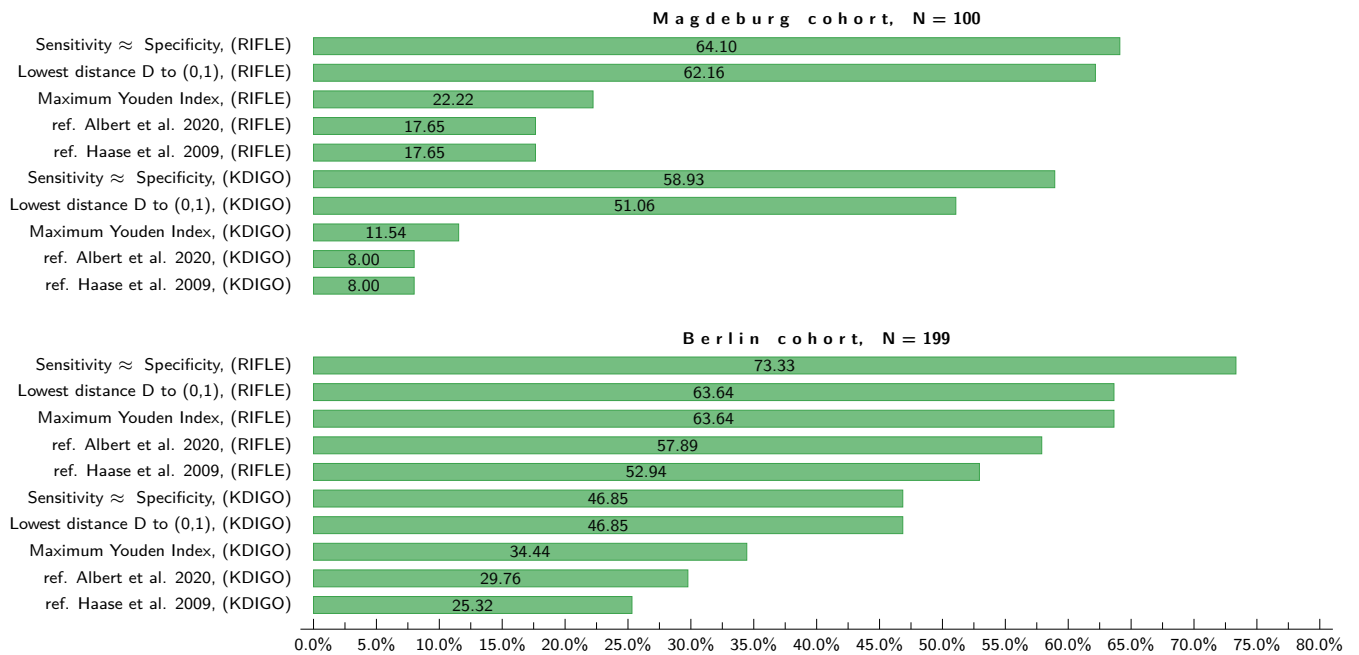
D) AUC-ROC for for NGAL predicting SCr/UO-based AKI according to the KDIGO criteria (N=59) in the Berlin cohort, N199; AUC = 0.632 (0.543 – 0.720), SE 0.045, $P = 0.003$.



Supplemental Data Figure 3:

We identified the proportion of patients with renal impairment additionally identified by urinary NGAL only in relation to the proportion of patients with AKI based on conventional RIFLE/KDIGO criteria adopting *formula 1*

$$\frac{\text{NGAL}(+)/\text{RIFLE}(-)}{\text{NGAL}(-)/\text{RIFLE}(+) + \text{NGAL}(+)/\text{RIFLE}(+)} \times 100 \quad (1)$$



Supplemental Data Figure 4:

In analogy to previous studies, we calculated the proportion of patients with renal impairment additionally identified by urinary NGAL only and not by RIFLE/KDIGO criteria (subclinical AKI, subfunctional AKI, AKI stage 1S) in relation to the proportion of patients diagnosed to have any renal impairment adopting *formula 2*

$$\frac{\text{NGAL}(+)/\text{RIFLE}(-)}{\text{NGAL}(+)/\text{RIFLE}(-) + \text{NGAL}(-)/\text{RIFLE}(+) + \text{NGAL}(+)/\text{RIFLE}(+)} \quad (2)$$

B) Odds Ratio fraction (magnitude of risk disparity): NGAL neg / sCr/UA pos vs. NGAL neg / sCr/UA neg (Ref.) groups for the outcome measures KRT-initiation, in-hospital mortality and KRT-initiation or in-hospital mortality

KRT - initiation

Berlin Cohort Odds Ratio : NGAL neg / sCr/UA pos vs. NGAL neg / sCr/UA neg (Ref.)

Cutoff methodology	AKI Classification	Cutoff value, ng/mL	Odds Ratio										
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	
			6,69	8,19	8,19	3,45	6,55	31,77	32,13	28,92	37,93	44,13	
Sensitivity = Specificity	RIFLE	16.85	6,69	1,00	1,22	1,22	0,52	0,98	4,75	4,80	4,33	5,67	6,60
Lowest distance D to (0,1)	RIFLE	50.0	8,19	0,82		1,00	0,42	0,80	3,88	3,92	3,53	4,63	5,39
Maximum Youden Index	RIFLE	50.0	8,19	0,82	1,00		0,42	0,80	3,88	3,92	3,53	4,63	5,39
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	3,45	1,94	2,37	2,37		1,90	9,21	9,31	8,38	10,99	12,79
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	149.25	6,55	1,02	1,25	1,25	0,53		4,85	4,91	4,42	5,79	6,74
Sensitivity = Specificity	KDIGO	14.25	31,77	0,21	0,26	0,26	0,11	0,21		1,01	0,91	1,19	1,39
Lowest distance D to (0,1)	KDIGO	14.75	32,13	0,21	0,25	0,25	0,11	0,20	0,99		0,90	1,18	1,37
Maximum Youden Index	KDIGO	36.5	28,92	0,23	0,28	0,28	0,12	0,23	1,10	1,11		1,31	1,53
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	37,93	0,18	0,22	0,22	0,09	0,17	0,84	0,85	0,76		1,16
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	149.25	44,13	0,15	0,19	0,19	0,08	0,15	0,72	0,73	0,66	0,86	

KRT - initiation

Magdeburg Cohort Odds Ratio : NGAL neg / sCr/UA pos vs. NGAL neg / sCr/UA neg (Ref.)

Cutoff methodology	AKI Classification	Cutoff value, ng/mL	Odds Ratio										
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	
			NC	NC	75,00	89,92	141,31	NC	NC	27,59	36,45	57,28	
Sensitivity = Specificity	RIFLE	10.6	NC	-	-	-	-	-	-	-	-	-	-
Lowest distance D to (0,1)	RIFLE	11.75	NC	-	-	-	-	-	-	-	-	-	-
Maximum Youden Index	RIFLE	45.55	75,00	-	-	1,20	1,88	-	-	-	0,37	0,49	0,76
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	89,92	-	-	0,83	1,57	-	-	-	0,31	0,41	0,64
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	159.1	141,31	-	-	0,53	0,64	-	-	-	0,20	0,26	0,41
Sensitivity = Specificity	KDIGO	8.0	NC	-	-	-	-	-	-	-	-	-	-
Lowest distance D to (0,1)	KDIGO	9.5	NC	-	-	-	-	-	-	-	-	-	-
Maximum Youden Index	KDIGO	45.55	27,59	-	-	2,72	3,26	5,12	-	-	-	1,32	2,08
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	36,45	-	-	2,06	2,47	3,88	-	-	-	0,76	1,57
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	159.1	57,28	-	-	1,31	1,57	2,47	-	-	-	0,48	0,64

In-hospital mortality

Berlin Cohort Odds Ratio : NGAL neg / sCr/VO pos vs. NGAL neg / sCr/VO neg (Ref.)

Cutoff methodology	AKI Classification	Cutoff value, ng/ml	OR									
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO
			30,86	37,71	37,71	17,38	14,50	8,70	8,80	8,00	6,65	6,38
Sensitivity = Specificity	RIFLE	16.85	30,86	1,22	1,22	0,56	0,47	0,28	0,29	0,26	0,22	0,21
Lowest distance D to (0,1)	RIFLE	50.0	37,71	0,82	1,00	0,46	0,38	0,23	0,23	0,21	0,18	0,17
Maximum Youden Index	RIFLE	50.0	37,71	0,82	1,00	0,46	0,38	0,23	0,23	0,21	0,18	0,17
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	17,38	1,78	2,17	2,17	0,83	0,50	0,51	0,46	0,38	0,37
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	149.25	14,50	2,13	2,60	2,60	1,20	0,60	0,61	0,55	0,46	0,44
Sensitivity = Specificity	KDIGO	14.25	8,70	3,55	4,33	4,33	2,00	1,67	1,01	0,92	0,76	0,73
Lowest distance D to (0,1)	KDIGO	14.75	8,80	3,51	4,29	4,29	1,97	1,65	0,99	0,91	0,76	0,72
Maximum Youden Index	KDIGO	36.5	8,00	3,86	4,71	4,71	2,17	1,81	1,09	1,10	0,83	0,80
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	6,65	4,64	5,67	5,67	2,61	2,18	1,31	1,32	1,20	0,96
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	149.25	6,38	4,84	5,91	5,91	2,72	2,27	1,36	1,38	1,25	1,04

In-hospital mortality

Magdeburg Cohort Odds Ratio : NGAL neg / sCr/VO pos vs. NGAL neg / sCr/VO neg (Ref.)

Cutoff methodology	AKI Classification	Cutoff value, ng/ml	OR									
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO
			NC	NC	38,08	55,67	43,95	NC	NC	15,41	24,35	21,57
Sensitivity = Specificity	RIFLE	10.6	NC	-	-	-	-	-	-	-	-	-
Lowest distance D to (0,1)	RIFLE	11.75	NC	-	-	-	-	-	-	-	-	-
Maximum Youden Index	RIFLE	45.55	38,08	-	-	1,46	1,15	-	-	0,40	0,64	0,57
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	55,67	-	-	0,68	0,79	-	-	0,28	0,44	0,39
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	159.1	43,95	-	-	0,87	1,27	-	-	0,35	0,55	0,49
Sensitivity = Specificity	KDIGO	8.0	NC	-	-	-	-	-	-	-	-	-
Lowest distance D to (0,1)	KDIGO	9.5	NC	-	-	-	-	-	-	-	-	-
Maximum Youden Index	KDIGO	45.55	15,41	-	-	2,47	3,61	2,85	-	-	1,58	1,40
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	24,35	-	-	1,56	2,29	1,80	-	-	0,63	0,89
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	159.1	21,57	-	-	1,77	2,58	2,04	-	-	0,71	1,13

KRT initiation or in-hospital mortality

Berlin Cohort

Odds Ratio : NGAL neg / sCr/UA pos vs. NGAL neg / sCr/UA neg (Ref.)

Cutoff methodology	AKI Classification		Cutoff value, ng/ml										
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	
			16.85	50.0	50.0	79.3	149.25	14.25	14.75	36.5	79.3	149.25	
		OR	10,10	12,38	12,38	8,50	10,52	19,33	19,56	17,28	12,76	14,30	
Sensitivity = Specificity	RIFLE	16.85	10,10		1,23	1,23	0,84	1,04	1,92	1,94	1,71	1,26	1,42
Lowest distance D to (0,1)	RIFLE	50.0	12,38	0,82		1,00	0,69	0,85	1,56	1,58	1,40	1,03	1,16
Maximum Youden Index	RIFLE	50.0	12,38	0,82	1,00		0,69	0,85	1,56	1,58	1,40	1,03	1,16
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	8,50	1,19	1,46	1,46		1,24	2,27	2,30	2,03	1,50	1,68
ref. Haase <i>et al.</i> [25] ^{##}	RIFLE	149.25	10,52	0,96	1,18	1,18	0,81		1,84	1,86	1,64	1,21	1,36
Sensitivity = Specificity	KDIGO	14.25	19,33	0,52	0,64	0,64	0,44	0,54		1,01	0,89	0,66	0,74
Lowest distance D to (0,1)	KDIGO	14.75	19,56	0,52	0,63	0,63	0,43	0,54	0,99		0,88	0,65	0,73
Maximum Youden Index	KDIGO	36.5	17,28	0,58	0,72	0,72	0,49	0,61	1,12	1,13		0,74	0,83
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	12,76	0,79	0,97	0,97	0,67	0,82	1,52	1,53	1,35		1,12
ref. Haase <i>et al.</i> [25] ^{##}	KDIGO	149.25	14,30	0,71	0,87	0,87	0,59	0,74	1,35	1,37	1,21	0,89	

KRT initiation or in-hospital mortality

Magdeburg Cohort

Odds Ratio : NGAL neg / sCr/UA pos vs. NGAL neg / sCr/UA neg (Ref.)

Cutoff methodology	AKI Classification		Cutoff value, ng/ml										
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	
			10.6	11.75	45.55	66.3	159.1	8.0	9.5	45.55	66.3	159.1	
		OR	NC	NC	75,00	89,92	141,31	NC	NC	27,59	36,45	57,28	
Sensitivity = Specificity	RIFLE	10.6	NC	-	-	-	-	-	-	-	-	-	-
Lowest distance D to (0,1)	RIFLE	11.75	NC	-	-	-	-	-	-	-	-	-	-
Maximum Youden Index	RIFLE	45.55	75,00	-	-	1,20	1,88	-	-	0,37	0,49	0,76	
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	89,92	-	-	0,83	1,57	-	-	0,31	0,41	0,64	
ref. Haase <i>et al.</i> [25] ^{##}	RIFLE	159.1	141,31	-	-	0,53	0,64	-	-	0,20	0,26	0,41	
Sensitivity = Specificity	KDIGO	8.0	NC	-	-	-	-	-	-	-	-	-	-
Lowest distance D to (0,1)	KDIGO	9.5	NC	-	-	-	-	-	-	-	-	-	-
Maximum Youden Index	KDIGO	45.55	27,59	-	-	2,72	3,26	5,12	-	-	1,32	2,08	
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	36,45	-	-	2,06	2,47	3,88	-	-	0,76	1,57	
ref. Haase <i>et al.</i> [25] ^{##}	KDIGO	159.1	57,28	-	-	1,31	1,57	2,47	-	-	0,48	0,64	

C) Odds Ratio fraction (magnitude of risk disparity): NGAL neg / sCr/UO pos vs. NGAL neg / sCr/UO neg (Ref.) groups for the outcome measures KRT-initiation, in-hospital mortality and KRT-initiation or in-hospital mortality

KRT - initiation												
Berlin Cohort												
Odds Ratio : NGAL pos / sCr/UO pos vs. NGAL neg / sCr/UO neg (Ref.)												

Cutoff methodology	AKI Classification	Cutoff value, ng/mL	OR										
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	
			16.85	50.0	50.0	79.3	149.25	14.25	14.75	36.5	79.3	149.25	
			46,81	57,31	57,31	40,25	43,20	67,58	68,35	112,17	145,44	157,17	
Sensitivity ≈ Specificity	RIFLE	16.85	46,81	1,22	1,22	0,86	0,92	1,44	1,46	2,40	3,11	3,36	
Lowest distance D to (0,1)	RIFLE	50.0	57,31	0,82	1,00	0,70	0,75	1,18	1,19	1,96	2,54	2,74	
Maximum Youden Index	RIFLE	50.0	57,31	0,82	1,00	0,70	0,75	1,18	1,19	1,96	2,54	2,74	
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	40,25	1,16	1,42	1,42		1,07	1,68	1,70	2,79	3,61	3,90
ref. Haase <i>et al.</i> [25] ^{##}	RIFLE	149.25	43,20	1,08	1,33	1,33	0,93		1,56	1,58	2,60	3,37	3,64
Sensitivity ≈ Specificity	KDIGO	14.25	67,58	0,69	0,85	0,85	0,60	0,64		1,01	1,66	2,15	2,33
Lowest distance D to (0,1)	KDIGO	14.75	68,35	0,68	0,84	0,84	0,59	0,63	0,99		1,64	2,13	2,30
Maximum Youden Index	KDIGO	36.5	112,17	0,42	0,51	0,51	0,36	0,39	0,60	0,61		1,30	1,40
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	145,44	0,32	0,39	0,39	0,28	0,30	0,46	0,47	0,77		1,08
ref. Haase <i>et al.</i> [25] ^{##}	KDIGO	149.25	157,17	0,30	0,36	0,36	0,26	0,27	0,43	0,43	0,71	0,93	

KRT - initiation												
Magdeburg Cohort												
Odds Ratio : NGAL pos / sCr/UO pos vs. NGAL neg / sCr/UO neg (Ref.)												

Cutoff methodology	AKI Classification	Cutoff value, ng/mL	OR										
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	
			10.6	11.75	45.55	66.3	159.1	8.0	9.5	45.55	66.3	159.1	
			177,67	183,44	212,14	233,80	100,20	77,13	92,73	149,00	151,00	64,71	
Sensitivity ≈ Specificity	RIFLE	10.6	177,67	1,03	1,19	1,32	0,56	0,43	0,52	0,84	0,85	0,36	
Lowest distance D to (0,1)	RIFLE	11.75	183,44	0,97	1,16	1,27	0,55	0,42	0,51	0,81	0,82	0,35	
Maximum Youden Index	RIFLE	45.55	212,14	0,84	0,86	1,10	0,47	0,36	0,44	0,70	0,71	0,31	
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	233,80	0,76	0,78	0,91	0,43	0,33	0,40	0,64	0,65	0,28	
ref. Haase <i>et al.</i> [25] ^{##}	RIFLE	159.1	100,20	1,77	1,83	2,12	2,33		0,77	0,93	1,49	1,51	0,65
Sensitivity ≈ Specificity	KDIGO	8.0	77,13	2,30	2,38	2,75	3,03	1,30		1,20	1,93	1,96	0,84
Lowest distance D to (0,1)	KDIGO	9.5	92,73	1,92	1,98	2,29	2,52	1,08	0,83		1,61	1,63	0,70
Maximum Youden Index	KDIGO	45.55	149,00	1,19	1,23	1,42	1,57	0,67	0,52	0,62		1,01	0,43
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	151,00	1,18	1,21	1,40	1,55	0,66	0,51	0,61	0,99		0,43
ref. Haase <i>et al.</i> [25] ^{##}	KDIGO	159.1	64,71	2,75	2,83	3,28	3,61	1,55	1,19	1,43	2,30	2,33	

In-hospital mortality

Berlin Cohort

Odds Ratio : NGAL pos / sCr/UO pos vs. NGAL neg / sCr/UO neg (Ref.)

Cutoff methodology	AKI Classification	Cutoff value, ng/mL	OR											
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO		
			16.85	50.0	50.0	79.3	149.25	14.25	14.75	36.5	79.3	149.25		
			72,00											
Sensitivity ≈ Specificity	RIFLE	16.85	72,00		1,22	1,22	0,40	0,56	0,33	0,34	0,55	0,31	0,41	
Lowest distance D to (0,1)	RIFLE	50.0	88,00	0,82		1,00	0,33	0,46	0,27	0,28	0,45	0,26	0,34	
Maximum Youden Index	RIFLE	50.0	88,00	0,82	1,00		0,33	0,46	0,27	0,28	0,45	0,26	0,34	
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	28,96	2,49	3,04	3,04		1,39	0,83	0,84	1,36	0,78	1,02	
ref. Haase <i>et al.</i> [25] ^{##}	RIFLE	149.25	40,28	1,79	2,18	2,18	0,72		0,60	0,60	0,98	0,56	0,73	
Sensitivity ≈ Specificity	KDIGO	14.25	24,00	3,00	3,67	3,67	1,21	1,68		1,01	1,64	0,94	1,23	
Lowest distance D to (0,1)	KDIGO	14.75	24,28	2,97	3,63	3,63	1,19	1,66	0,99		1,62	0,93	1,22	
Maximum Youden Index	KDIGO	36.5	39,27	1,83	2,24	2,24	0,74	1,03	0,61	0,62		0,58	0,75	
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	22,60	3,19	3,89	3,89	1,28	1,78	1,06	1,07	1,74		1,31	
ref. Haase <i>et al.</i> [25] ^{##}	KDIGO	149.25	29,50	2,44	2,98	2,98	0,98	1,37	0,81	0,82	1,33	0,77		

In-hospital mortality

Magdeburg Cohort

Odds Ratio : NGAL pos / sCr/UO pos vs. NGAL neg / sCr/UO neg (Ref.)

Cutoff methodology	AKI Classification	Cutoff value, ng/mL	OR											
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO		
			10.6	11.75	45.55	66.3	159.1	8.0	9.5	45.55	66.3	159.1		
			57,40											
Sensitivity ≈ Specificity	RIFLE	10.6	57,40		1,03	1,05	0,65	1,16	0,52	0,62	1,00	0,72	1,13	
Lowest distance D to (0,1)	RIFLE	11.75	59,27	0,97		1,01	0,63	1,13	0,50	0,60	0,97	0,69	1,09	
Maximum Youden Index	RIFLE	45.55	60,00	0,96	0,99		0,62	1,11	0,49	0,59	0,96	0,69	1,08	
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	37,11	1,55	1,60	1,62		1,80	0,80	0,96	1,54	1,11	1,74	
ref. Haase <i>et al.</i> [25] ^{##}	RIFLE	159.1	66,80	0,86	0,89	0,90	0,56		0,44	0,53	0,86	0,62	0,97	
Sensitivity ≈ Specificity	KDIGO	8.0	29,67	1,93	2,00	2,02	1,25	2,25		1,20	1,93	1,39	2,18	
Lowest distance D to (0,1)	KDIGO	9.5	35,67	1,61	1,66	1,68	1,04	1,87	0,83		1,61	1,15	1,81	
Maximum Youden Index	KDIGO	45.55	57,31	1,00	1,03	1,05	0,65	1,17	0,52	0,62		0,72	1,13	
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	41,18	1,39	1,44	1,46	0,90	1,62	0,72	0,87	1,39		1,57	
ref. Haase <i>et al.</i> [25] ^{##}	KDIGO	159.1	64,71	0,89	0,92	0,93	0,57	1,03	0,46	0,55	0,89	0,64		

KRT initiation or in-hospital mortality

Berlin Cohort

Odds Ratio : NGAL pos / sCr/UA pos vs. NGAL neg / sCr/UA neg (Ref.)

Cutoff methodology	AKI Classification		Cutoff value, ng/mL									
	RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO	
	16.85	50.0	50.0	79.3	149.25	14.25	14.75	36.5	79.3	149.25		
		OR	97,17	119,17	119,17	75,56	106,50	52,96	53,57	94,50	62,15	73,75
Sensitivity = Specificity	RIFLE	16.85	97,17	1,23	1,23	0,78	1,10	0,55	0,55	0,97	0,64	0,76
Lowest distance D to (0,1)	RIFLE	50.0	119,17	0,82	1,00	0,63	0,89	0,44	0,45	0,79	0,52	0,62
Maximum Youden Index	RIFLE	50.0	119,17	0,82	1,00	0,63	0,89	0,44	0,45	0,79	0,52	0,62
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	75,56	1,29	1,58	1,58	1,41	0,70	0,71	1,25	0,82	0,98
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	149.25	106,50	0,91	1,12	1,12	0,71	0,50	0,50	0,89	0,58	0,69
Sensitivity = Specificity	KDIGO	14.25	52,96	1,83	2,25	2,25	1,43	2,01	1,01	1,78	1,17	1,39
Lowest distance D to (0,1)	KDIGO	14.75	53,57	1,81	2,22	2,22	1,41	1,99	0,99	1,76	1,16	1,38
Maximum Youden Index	KDIGO	36.5	94,50	1,03	1,26	1,26	0,80	1,13	0,56	0,57	0,66	0,78
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	62,15	1,56	1,92	1,92	1,22	1,71	0,85	0,86	1,52	1,19
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	149.25	73,75	1,32	1,62	1,62	1,02	1,44	0,72	0,73	1,28	0,84

KRT initiation or in-hospital mortality

Magdeburg Cohort

Odds Ratio : NGAL pos / sCr/UA pos vs. NGAL neg / sCr/UA neg (Ref.)

Cutoff methodology	AKI Classification		Cutoff value, ng/mL									
	RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO		
	10.6	11.75	45.55	66.3	159.1	8.0	9.5	45.55	66.3	159.1		
		OR	177,67	183,44	212,14	233,80	100,20	77,13	92,73	149,00	151,00	64,71
Sensitivity = Specificity	RIFLE	10.6	177,67	1,03	1,19	1,32	0,56	0,43	0,52	0,84	0,85	0,36
Lowest distance D to (0,1)	RIFLE	11.75	183,44	0,97	1,16	1,27	0,55	0,42	0,51	0,81	0,82	0,35
Maximum Youden Index	RIFLE	45.55	212,14	0,84	0,86	1,10	0,47	0,36	0,44	0,70	0,71	0,31
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	233,80	0,76	0,78	0,91	0,43	0,33	0,40	0,64	0,65	0,28
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	159.1	100,20	1,77	1,83	2,12	2,33	0,77	0,93	1,49	1,51	0,65
Sensitivity = Specificity	KDIGO	8.0	77,13	2,30	2,38	2,75	3,03	1,30	1,20	1,93	1,96	0,84
Lowest distance D to (0,1)	KDIGO	9.5	92,73	1,92	1,98	2,29	2,52	1,08	0,83	1,61	1,63	0,70
Maximum Youden Index	KDIGO	45.55	149,00	1,19	1,23	1,42	1,57	0,67	0,52	0,62	1,01	0,43
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	151,00	1,18	1,21	1,40	1,55	0,66	0,51	0,61	0,99	0,43
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	159.1	64,71	2,75	2,83	3,28	3,61	1,55	1,19	1,43	2,30	2,33

D) Odds Ratio fraction (magnitude of risk disparity): NGAL pos / sCr/UA pos vs. NGAL neg / sCr/UA pos groups for the outcome measures KRT-initiation, in-hospital mortality and KRT-initiation or in-hospital mortality

KRT - initiation												
Berlin Cohort												
Odds Ratio : NGAL pos / sCr/UA pos vs. NGAL neg / sCr/UA pos												
Cutoff methodology	AKI Classification	Cutoff value, ng/ml	OR									
			7,00	7,00	7,00	11,67	6,60	2,13	2,13	3,88	3,84	3,56
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO
Sensitivity = Specificity	RIFLE	16.85	7,00	1,00	1,00	1,67	0,94	0,30	0,30	0,55	0,55	0,51
Lowest distance D to (0,1)	RIFLE	50.0	7,00	1,00	1,00	1,67	0,94	0,30	0,30	0,55	0,55	0,51
Maximum Youden Index	RIFLE	50.0	7,00	1,00	1,00	1,67	0,94	0,30	0,30	0,55	0,55	0,51
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	11,67	0,60	0,60	0,60	1,67	0,57	0,18	0,18	0,33	0,31
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	149.25	6,60	1,06	1,06	1,06	1,77	0,32	0,32	0,59	0,58	0,54
Sensitivity = Specificity	KDIGO	14.25	2,13	3,29	3,29	3,29	5,48	3,10	1,00	1,82	1,80	1,67
Lowest distance D to (0,1)	KDIGO	14.75	2,13	3,29	3,29	3,29	5,48	3,10	1,00	1,82	1,80	1,67
Maximum Youden Index	KDIGO	36.5	3,88	1,81	1,81	1,81	3,01	1,70	0,55	0,55	0,99	0,92
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	3,84	1,83	1,83	1,83	3,04	1,72	0,55	0,55	1,01	0,93
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	149.25	3,56	1,97	1,97	1,97	3,28	1,85	0,60	0,60	1,09	1,08

KRT - initiation												
Magdeburg Cohort												
Odds Ratio : NGAL pos / sCr/UA pos vs. NGAL neg / sCr/UA pos												
Cutoff methodology	AKI Classification	Cutoff value, ng/ml	OR									
			13,00	13,00	2,83	2,60	0,71	18,20	18,20	5,40	4,14	1,13
			RIFLE	RIFLE	RIFLE	RIFLE	RIFLE	KDIGO	KDIGO	KDIGO	KDIGO	KDIGO
Sensitivity = Specificity	RIFLE	10.6	13,00	1,00	0,22	0,20	0,05	1,40	1,40	0,42	0,32	0,09
Lowest distance D to (0,1)	RIFLE	11.75	13,00	1,00	0,22	0,20	0,05	1,40	1,40	0,42	0,32	0,09
Maximum Youden Index	RIFLE	45.55	2,83	4,60	4,60	0,92	0,25	6,43	6,43	1,91	1,46	0,40
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	2,60	5,00	5,00	1,09	0,27	7,00	7,00	2,08	1,59	0,43
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	159.1	0,71	18,33	18,33	3,99	3,67	25,67	25,67	7,62	5,84	1,59
Sensitivity = Specificity	KDIGO	8.0	18,20	0,71	0,71	0,16	0,14	0,04	1,00	0,30	0,23	0,06
Lowest distance D to (0,1)	KDIGO	9.5	18,20	0,71	0,71	0,16	0,14	0,04	1,00	0,30	0,23	0,06
Maximum Youden Index	KDIGO	45.55	5,40	2,41	2,41	0,52	0,48	0,13	3,37	3,37	0,77	0,21
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	4,14	3,14	3,14	0,68	0,63	0,17	4,39	4,39	1,30	0,27
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	159.1	1,13	11,51	11,51	2,50	2,30	0,63	16,11	16,11	4,78	3,67

KRT initiation or in-hospital mortality

Berlin Cohort

Odds Ratio : NGAL pos / sCr/UO pos vs. NGAL neg / sCr/UO pos

Cutoff methodology	AKI Classification		Cutoff value, ng/mL									
	RIFLE	KDIGO	16.85	50.0	50.0	79.3	149.25	14.25	14.75	36.5	79.3	149.25
	OR		9,63	9,63	9,63	8,89	10,13	2,74	2,74	5,47	4,87	5,16
Sensitivity = Specificity	RIFLE	16.85	9,63	1,00	1,00	0,92	1,05	0,28	0,28	0,57	0,51	0,54
Lowest distance D to (0,1)	RIFLE	50.0	9,63	1,00	1,00	0,92	1,05	0,28	0,28	0,57	0,51	0,54
Maximum Youden Index	RIFLE	50.0	9,63	1,00	1,00	0,92	1,05	0,28	0,28	0,57	0,51	0,54
ref. Albert <i>et al.</i> [9] [#]	RIFLE	79.3	8,89	1,08	1,08	1,08	1,14	0,31	0,31	0,62	0,55	0,58
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	149.25	10,13	0,95	0,95	0,95	0,88	0,27	0,27	0,54	0,48	0,51
Sensitivity = Specificity	KDIGO	14.25	2,74	3,51	3,51	3,51	3,25	3,70	1,00	2,00	1,78	1,88
Lowest distance D to (0,1)	KDIGO	14.75	2,74	3,51	3,51	3,51	3,25	3,70	1,00	2,00	1,78	1,88
Maximum Youden Index	KDIGO	36.5	5,47	1,76	1,76	1,76	1,63	1,85	0,50	0,50	0,89	0,94
ref. Albert <i>et al.</i> [9] [#]	KDIGO	79.3	4,87	1,98	1,98	1,98	1,82	2,08	0,56	0,56	1,12	1,06
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	149.25	5,16	1,87	1,87	1,87	1,72	1,96	0,53	0,53	1,06	0,94

KRT initiation or in-hospital mortality

Magdeburg Cohort

Odds Ratio : NGAL pos / sCr/UO pos vs. NGAL neg / sCr/UO pos

Cutoff methodology	AKI Classification		Cutoff value, ng/mL									
	RIFLE	KDIGO	10.6	11.75	45.55	66.3	159.1	8.0	9.5	45.55	66.3	159.1
	OR		13,00	13,00	2,83	2,60	0,71	18,20	18,20	5,40	4,14	1,13
Sensitivity = Specificity	RIFLE	10.6	13,00	1,00	0,22	0,20	0,05	1,40	1,40	0,42	0,32	0,09
Lowest distance D to (0,1)	RIFLE	11.75	13,00	1,00	0,22	0,20	0,05	1,40	1,40	0,42	0,32	0,09
Maximum Youden Index	RIFLE	45.55	2,83	4,60	4,60	0,92	0,25	6,43	6,43	1,91	1,46	0,40
ref. Albert <i>et al.</i> [9] [#]	RIFLE	66.3	2,60	5,00	5,00	1,09	0,27	7,00	7,00	2,08	1,59	0,43
ref. Haase <i>et al.</i> [25] ^{###}	RIFLE	159.1	0,71	18,33	18,33	3,99	3,67	25,67	25,67	7,62	5,84	1,59
Sensitivity = Specificity	KDIGO	8.0	18,20	0,71	0,71	0,16	0,14	0,04	1,00	0,30	0,23	0,06
Lowest distance D to (0,1)	KDIGO	9.5	18,20	0,71	0,71	0,16	0,14	0,04	1,00	0,30	0,23	0,06
Maximum Youden Index	KDIGO	45.55	5,40	2,41	2,41	0,52	0,48	0,13	3,37	3,37	0,77	0,21
ref. Albert <i>et al.</i> [9] [#]	KDIGO	66.3	4,14	3,14	3,14	0,68	0,63	0,17	4,39	4,39	1,30	0,27
ref. Haase <i>et al.</i> [25] ^{###}	KDIGO	159.1	1,13	11,51	11,51	2,50	2,30	0,63	16,11	16,11	4,78	3,67