Appendix 1a. Prediction of severe AKI by biomarker composites

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	22 (13-35)	94 (91-96)	45 (27-64)	85 (80-89)	3.8 (1.9-7.2)	0.8 (0.7-0.9)
uNGAL- pCysC -	3 (0-11)	46 (40-52)	1 (0-5)	69 (61-75)	0.1 (0-0.2)	2.1 (1.8-2.4)
uNGAL- pCysC +	8 (3-18)	59 (53-65)	4 (1-9)	75 (68-80)	0.2 (0.1-0.5)	1.6 (1.4-1.8)
uNGAL+ pCysC -	26 (15-39)	99 (96-100)	18 (14-22)	86 (82-89)	18.3 (6.3-52.7)	0.8 (0.7-0.9)
uNGAL+ pCysC +	63 (50-75)	96 (93-98)	78 (64-88)	92 (89-95)	16.2 (8.8-29.8)	0.4 (0.3-0.5)

Appendix 1b. Prediction of AKI duration by biomarker composites

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	31 (15-51)	93 (90-96)	29 (14-48)	93 (90-96)	4.5 (2.3-8.8)	0.7 (0.6-0.9)
uNGAL- pCysC -	4 (0-18)	52 (46-57)	1 (0-4)	85 (80-90)	0.1 (0-0.5)	1.9 (1.7-2.1)
uNGAL- pCysC +	0 (0-12)	62 (56-67)	0 (0-3)	87 (82-91)	0	1.6 (1.5-1.8)
uNGAL+ pCysC -	28 (13-47)	96 (93-98)	40 (19-64)	94 (90-96)	7.3 (3.2-16.3)	0.8 (0.6-0.9)
uNGAL+ pCysC +	69 (49-85)	91 (87-94)	40 (26-55)	97 (94-99)	7.3 (4.8-11.0)	0.3 (0.2-0.6)

Biomarker composites of urinary neutrophil gelatinase associated lipocalin (uNGAL) measured at 6 hours and plasma Cystatin C (pCysC) measured at 2 hours in relation to their respective cut-off values for positivity ≥ 200 ng and 0.8 mg/L (+) demonstrate improved prediction of severe acute kidney injury (AKI) characteristics compared to the change in serum creatinine (Δ SCr) from pre-operative to first post-operative value (cut-off value for positivity of ≥ 50% increase). uNGAL is normalized to urinary creatinine. PPV = positive predictive value, NPV = negative predictive value, LR = likelihood ratio. Sensitivity, specificity, PPV, and NPV are depicted as percentages. All values are listed with 95% confidence intervals.

Appendix 2a. Prediction of severe AKI by biomarker composites including non-normalized uNGAL

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	22 (13-35)	94 (91-96)	45 (27-64)	85 (80-89)	3.8 (1.9-7.2)	0.8 (0.7-0.9)
uNGAL- pCysC -	3 (0.5-11)	48 (42-54)	1 (0-5)	69 (62-76)	0.1 (0.0-0.2)	2.0 (1.8-2.3)
uNGAL- pCysC +	13 (6-24)	59 (53-65)	6 (3-12)	75 (69-81)	0.3 (0.2-0.6)	1.5 (1.3-1.7)
uNGAL+ pCysC -	26 (15-39)	97 (94-99)	64 (42-82)	86 (81-89)	8.1 (3.8-17.5)	0.8 (0.7-0.9)
uNGAL+ pCysC +	58 (45-70)	97 (94-98)	78 (63-89)	91 (88-94)	16.4 (8.6-31.3)	0.4 (0.3-0.6)

Appendix 2b. Prediction of AKI > 2 days by biomarker composites including non-normalized uNGAL

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	31 (15-51)	93 (90-96)	29 (14-48)	93 (90-96)	4.5 (2.3-8.8)	0.7 (0.6-0.9)
uNGAL- pCysC -	0 (0-12)	53 (47-58)	0 (0-2)	85 (79-90)	0	1.9 (1.7-2.1)
uNGAL- pCysC +	0 (0-12)	60 (55-66)	0 (0-3)	87 (82-91)	0	1.7 (1.5-1.8)
uNGAL+ pCysC -	31 (15-51)	95 (92-97)	36 (18-57)	94 (91-96)	6.1 (2.9-12.6)	0.7 (0.6-0.9)
uNGAL+ pCysC +	69 (49-85)	92 (88-95)	43 (29-59)	97 (94-99)	8.4 (5.4-13.0)	0.3 (0.2-0.6)

Biomarker composites of urinary neutrophil gelatinase associated lipocalin (uNGAL) and plasma Cystatin C (pCysC) in relation to their respective cut-off values for positivity $\geq$ 100 ng and 0.8 mg/L (+) demonstrate significantly improved prediction of acute kidney injury (AKI) severity (A) and duration > 2 days (b) compared to the change in serum creatinine (Δ SCr) from pre-operative to first post-operative value (cut-off value for positivity of $\geq$ 50% increase). uNGAL is not normalized to urine creatinine. PPV = positive predictive value, NPV = negative predictive value, LR = likelihood ratio. Sensitivity, specificity, PPV, and NPV are depicted as percentages. All values are listed with 95% confidence intervals.

Appendix 3a. Prediction of severe AKI by biomarker composites using pCysC

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	22 (13-35)	94 (91-96)	45 (27-64)	85 (80-89)	3.8 (1.9-7.2)	0.8 (0.7-0.9)
uNGAL- pCysC -	5 (1-14)	46 (41-52)	2 (0-6)	69 (62-76)	0.1 (0-0.3)	2.0 (1.8-2.3)
uNGAL- pCysC +	23 (13-35)	57 (50-63)	10 (6-17)	77 (71-82)	0.5 (0.3-0.8)	1.4 (1.2-1.6)
uNGAL+ pCysC -	24 (14-37)	98 (96-99)	75 (51-91)	75 (51-91)	13.7 (5-36)	0.8 (0.7-0.9)
uNGAL+ pCysC +	48 (36-61)	99 (96-100)	88 (73-97)	90 (86-93)	34.2 (13-94)	0.5 (0.4-0.7)

Appendix 3b. Prediction of severe AKI by biomarker composites using Δ SCr

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	22 (13-35)	94 (91-96)	45 (27-64)	85 (80-89)	3.8 (1.9-7.2)	0.8 (0.7-0.9)
uNGAL- Δ SCr -	19 (10-31)	8 (5-12)	4 (2-8)	31 (20-43)	0.2 (0.1-0.4)	10.4 (6.8-15.8)
uNGAL- Δ SCr +	8 (3-18)	95 (93-98)	28 (10-53)	83 (78-87)	1.8 (0.7-4.7)	1.0 (0.9-1.0)
uNGAL+ Δ SCr -	47 (34-60)	98 (96-99)	85 (69-95)	89 (85-93)	26.5 (10.7-65.7)	0.5 (0.4-0.7)
uNGAL+ Δ SCr +	26 (15-39)	99 (96-100)	80 (56-94)	86 (82-89)	18.3 (6.3-53)	0.8 (0.7-0.9)

Appendix 3c. Prediction of AKI > 2 days by biomarker composites using pCysC

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	31 (15-51)	93 (90-96)	29 (14-48)	93 (90-96)	4.5 (2.3-8.8)	0.7 (0.6-0.9)
uNGAL- pCysC -	7 (1-23)	52 (46-58)	1.3 (0.2-4.6)	86 (80-90)	0.1 (0-0.6)	1.8 (1.5-2.0)
uNGAL- pCysC +	0 (0-16)	57 (51-62)	0 (0-3)	89 (83-93)	0 (nc)	1.8 (1.6-1.9)
uNGAL+ pCysC -	24 (10-44)	96 (93-98)	35 (15-59)	93 (90-96)	5.9 (2.5-13.5)	0.8 (0.6-1.0)
uNGAL+ pCysC +	69 (49-85)	96 (93-98)	59 (41-75)	97 (95-99)	15.6 (8.8-27.5)	0.3 (0.2-0.6)

Appendix 3d. Prediction of AKI > 2 days by biomarker composites using Δ SCr

Marker	Sensitivity	Specificity	PPV	NPV	+ LR	- LR
Δ SCr +	31 (15-51)	93 (90-96)	29 (14-48)	93 (90-96)	4.5 (2.3-8.8)	0.7 (0.6-0.9)
uNGAL- Δ SCr -	3 (0-18)	14 (10-18)	0 (0-2)	61 (49-73)	0 (0-0.3)	6.9 (5.2-9.2)
uNGAL- Δ SCr +	3 (0-18)	95 (92-97)	6 (1-27)	91 (88-94)	0.6 (0.1-4.7)	1.0 (0.9-1.1)
uNGAL+ Δ SCr -	59 (39-76)	95 (92-97)	50 (32-68)	96 (94-98)	10.9 (6.3-18.9)	0.4 (0.3-0.7)
uNGAL+ Δ SCr +	35 (18-54)	97 (94-98)	50 (27-73)	94 (91-96)	10.9 (4.9-24.0)	0.7 (0.5-0.9)

Biomarker composites of urinary neutrophil gelatinase associated lipocalin (uNGAL) and plasma Cystatin C (pCysC) measured in relation to their respective cut-off values for positivity $\geq$ 200 ng and 0.8 mg/L (+) (3a and 3c) vs. uNGAL combined with Δ SCr (3b and 3d) (change in serum creatinine from pre-operative to first post-operative value (cut-off value for positivity of $\geq$ 50% increase) for prediction of severe acute kidney injury (AKI) (3a/3b) and AKI > 2 days (3c/3d). uNGAL is normalized to urinary creatinine. PPV = positive predictive value, NPV = negative predictive value, LR = likelihood ratio. Sensitivity, specificity, PPV, and NPV are depicted as percentages. All values are listed with 95% confidence intervals.