Supplemental Material

Table S1. Characteristics of the study dataset, stratified by CKD stage.

	CKD 3	CKD 4	CKD 5 ND	p
n (% of all CKD cases)	246 (88%)	24 (9%)	10 (3%)	
Age, mean (SD)	71.9 (8.8)	76.5 (7.2)	65.4 (11.4)	0.003
Female, n (%)	104 (42%)	13 (54%)	2 (20%)	0.181
eGFR (ml/min/1.73 m²), mean (SD)	49.4 (7.9)	24.4 (3.8)	9.2 (3.6)	<0.001
NSTEMI, n (%)	57 (23%)	10 (42%)	6 (60%)	0.006
Hypertension, n (%)	236 (96%)	24 (100%)	10 (100%)	0.488
Diabetes, n (%)	81 (33%)	11 (46%)	2 (20%)	0.288
Initial hs-cTnI (ng/L), median (IQR)	12.7 (6.1, 58.9)	51.3 (17.7, 180.1)	128.8 (55.2, 575.9)	<0.001
Second hs-cTnI (ng/L), median (IQR)	15.0 (8.6, 88.2)	54.9 (20.8, 257.8)	100.3, (43.7, 631.0)	0.021

Baseline characteristics of CKD patients (study dataset), stratified by CKD stadium).CKD, chronic kidney disease; ND, not on dialysis

Table S2. Characteristics of the clinical dataset, stratified by CKD stage.

	CKD 3	CKD 4	CKD 5 ND	p
n (% of all CKD cases)	1333 (84%)	216 (14%)	32 (2%)	
Age, mean (SD)	77.1 (9.5)	79.9 (9.2)	68.2 (14.0)	<0.001
Female, n (%)	568 (43)	118 (55)	10 (31)	0.001
eGFR (ml/min/1.73 m²), mean (SD)	49.7 (18.1)	30.8 (14.7)	15.3 (18.7)	<0.001
NSTEMI, n (%)	372 (28%)	68 (32%)	6 (19%)	0.27
Hypertension, n (%)	1152 (86%)	198 (92%)	27 (84%)	0.09
Diabetes, n (%)	490 (37%)	97 (45%)	14 (44%)	0.06
Initial hs-cTnT (ng/L), median (IQR)	27.6 (15.1, 59.8)	44.5 (22.8, 100.1)	92.2 (49.1, 145.2)	<0.001
Second hs-cTnT (ng/L), median (IQR)	33.2 (16.3, 96.5)	53.8 (25.7, 135.5)	105.8 (52.2, 237.7)	<0.001

Baseline characteristics of CKD patients (clinical dataset), stratified by CKD stadium).CKD, chronic kidney disease; ND, not on dialysis

Table S3. Number of patients undergoing percutaneous intervention or coronary bypass grafting in the study dataset.

No NSTEMI	Non-CKD patients	CKD patients	p
CABG, x/n (%)	9/1036 (0.9)	2/207 (1.0)	1.000
PCI, x/n (%)	93/1036 (9.0)	18/207 (8.7)	1.000
NSTEMI			
CABG, x/n (%)	17/178 (9.6)	13/73 (17.8)	0.106
PCI, x/n (%)	139/178 (78.1)	45/73 (61.6)	0.008

CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention. Statistical significance was asserted by Chi-squared test.

Table S4. Number of patients undergoing percutaneous intervention or coronary bypass grafting in the clinical dataset.

No NSTEMI	Non-CKD patients	CKD patients	p
CABG, x/n (%)	0/4549 (0)	2/1135 (1.8)	0.052
PCI, x/n (%)	172/4549 (3.8)	86/1135 (7.6)	< 0.001
NSTEMI			
CABG, x/n (%)	10/929 (1.1)	7/446 (1.6)	0.607
PCI, x/n (%)	534/929 (57.5)	209/446 (46.9)	< 0.001

CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention. Statistical significance was asserted by Chi-squared test.

Table S5. Diagnostic performances of conventional and optimized cut-offs for second troponin measurements in CKD patients.

hs-cTnI	Sensitivity	Specificity	LR+	LR-	PPV	NPV
30 ng/L	0.97 (0.9, 1)	0.80 (0.74, 0.85)	4.74 (3.63, 6.19)	0.04 (0.01, 0.15)	0.60 (0.5, 0.69)	0.99 (0.96, 1)
54.0 ng/L	0.96 (0.88, 0.99)	0.86 (0.81, 0.9)	6.85 (4.9, 9.58)	0.05 (0.02, 0.16)	0.68 (0.58, 0.78)	0.98 (0.95, 1)
150 ng/L	0.87 (0.76, 0.94)	0.96 (0.93, 0.98)	23.32 (11.7, 46.3)	0.14 (0.07, 0.25)	0.88 (0.78, 0.95)	0.96 (0.92, 0.98)
hs-cTnT	**Sensitivity**	**Specificity**	**LR+**	**LR-**	**PPV**	**NPV**
14 ng/L	0.95 (0.93, 0.97)	0.24 (0.22, 0.27)	1.25 (1.21, 1.3)	0.2 (0.13, 0.31)	0.33 (0.3, 0.36)	0.93 (0.89, 0.95)
50 ng/L	0.84 (0.81, 0.88)	0.76 (0.74, 0.79)	3.56 (3.18, 3.98)	0.21 (0.17, 0.26)	0.58 (0.54, 0.62)	0.93 (0.91, 0.94)
70 ng/L	0.76 (0.72, 0.8)	0.86 (0.84, 0.88)	5.41 (4.64, 6.3)	0.28 (0.23, 0.33)	0.68 (0.64, 0.72)	0.9 (0.88, 0.92)

CKD, chronic kidney disease; hs-cTnI, high-sensitive troponin I; hs-cTnT, high-sensitive troponin T; LR+, positive likelihood ratio; LR-, negative likelihood ratio; PPV, positive predictive value; NPV, negative predictive value.

Table S6. Changes in serial troponin levels.

	Study dataset (troponin I)			Clinical dataset (troponin T)		
Difference	**No CKD**	**CKD**	**p**	**No CKD**	**CKD**	**p**
No AMI	2.9 (1.9, 4)	3.1 (1.8, 5.8)	0.229	1.6 (0.6, 4.5)	3.5 (1.3, 9.6)	<0.001
AMI	447.6 (141.4, 1831)	330.4 (134.5, 683.2)	0.174	68.4 (17.9, 229.5)	80.6 (29.5, 301.6)	0.047
Relative Change	**No CKD**	**CKD**	**p**	**No CKD**	**CKD**	**p**
No AMI	1.7 (1.3, 2.4)	1.4 (1.1, 2)	<0.001	1.1 (1.1, 1.4)	1.1 (1.1, 1.4)	0.85
AMI	3.8 (1.5, 8.9)	2.2 (1.4, 6)	0.204	2.1 (1.3, 5.0)	2.2 (1.3, 5.0)	0.873

Values are expressed in ng/L as median and interquartile ranges. Only cases with rising troponin levels were included in this analysis (1185 of 1494 cases in the study dataset and 1944 of 4478 cases in the clinical dataset; cf. Tables 1 and 2). AMI, acute myocardial infarction; CKD, chronic kidney disease.

Table S7. Absolute (unsigned) changes in troponin levels.

hs-cTnI, differences	no CKD	CKD	p
Non AMI	2.8 (1.7, 4.1)	3 (1.3, 6.1)	0.355
AMI	430.3 (118.7, 1644)	251.7 (76.4, 658.7)	0.012
hs-cTnI, relative change	**no CKD**	**CKD**	**p**
Non AMI	57% (24%, 128%)	24% (10%, 73%)	<0.001
AMI	149% (18%, 574%)	76% (18%, 397%)	0.104
hs-cTnT, differences	**no CKD**	**CKD**	**p**
Non AMI	0.7 (0, 2.3)	2.7 (1, 6.9)	<0.001
AMI	47.6 (10.6, 191.3)	67.9 (19.2, 233.7)	0.024
hs-cTnT, relative change	**no CKD**	**CKD**	**p**
Non AMI	6% (0%, 18%)	10% (4%, 23%)	0.074
AMI	57% (11%, 256%)	65% (11%, 274%)	0.787

Absolute (unsigned) differences and corresponding relative changes of serial hs-cTn measurements. Because a rise or fall in troponin levels may indicate myocardial infarction, absolute values of the differences between the second and the first measurement were averaged; results expressed in ng/L with median and interquartile ranges. Relative changes were computed by dividing the larger value by the smaller value and subtract 1; the results are given as mean percent with interquartile ranges.

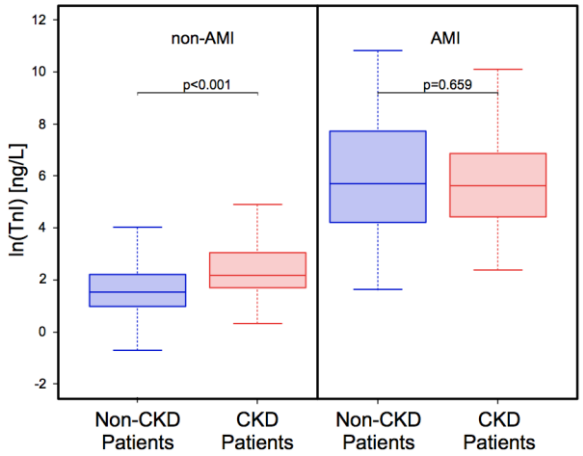
Table S8. Diagnostic performance of absolute (unsigned) changes in troponin levels in CKD patients.

hs-cTnI	Change	Sensitivity	Specificity	PPV	NPV
Baseline ≤ 30 pg/ml	12.62 ng/L	0.8 (0.28, 0.99)	0.96 (0.91, 0.98)	0.36 (0.11, 0.69)	0.99 (0.96, 1)
	160%	0.6 (0.15, 0.95)	0.89 (0.83, 0.94)	0.15 (0.03, 0.38)	0.99 (0.95, 1)
Baseline > 30 pg/ml	12.62 ng/L	0.87 (0.75, 0.95)	0.62 (0.44, 0.79)	0.79 (0.67, 0.89)	0.74 (0.54, 0.89)
	160%	0.3 (0.18, 0.44)	0.94 (0.79, 0.99)	0.89 (0.65, 0.99)	0.45 (0.33, 0.57)
hs-cTnT	**Change**	Sensitivity	Specificity	**PPV**	**NPV**
Baseline ≤ 14 pg/ml	21.86 ng/L	0.69 (0.48, 0.86)	0.95 (0.92, 0.97)	0.56 (0.38, 0.74)	0.97 (0.95, 0.99)
	77%	0.81 (0.61, 0.93)	0.85 (0.81, 0.89)	0.33 (0.22, 0.46)	0.98 (0.96, 0.99)
Baseline > 14 pg/ml	21.86 ng/L	0.74 (0.69, 0.78)	0.88 (0.86, 0.90)	0.76 (0.71, 0.8)	0.87 (0.85, 0.89)
	77%	0.45 (0.4, 0.5)	0.92 (0.9, 0.93)	0.73 (0.67, 0.78)	0.77 (0.74, 0.8)

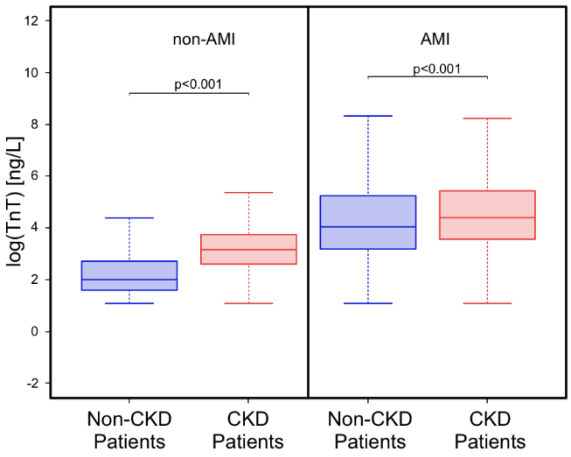
For this analysis, all changes between the first and second measurements were converted to absolute (unsigned) values.

Figure S1. Initial troponin levels.

A) Study dataset



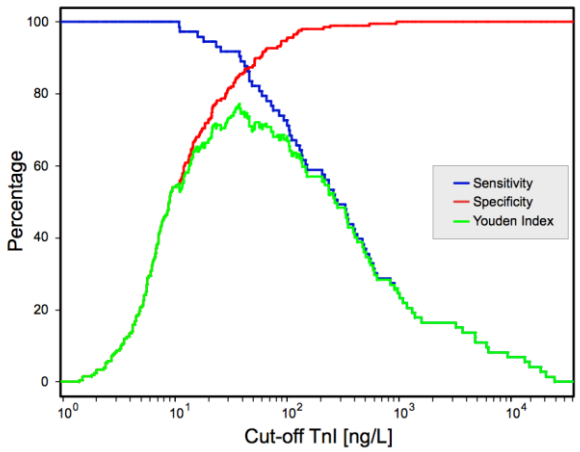
B) Clinical dataset



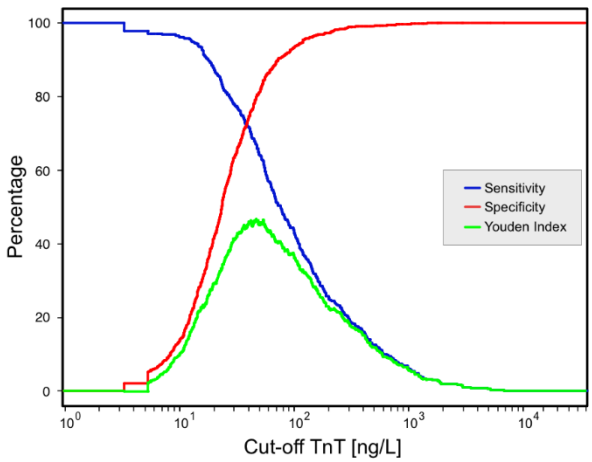
(A) hs-cTnI and **(B)** hs-cTnT levels upon admission in patients with acute chest pain divided according to renal function (eGFR, estimated glomerular filtration rate) and final diagnosis.

Figure S2. Sensitivity and specificity of initial troponins for the diagnosis of NSTE-AMI

A) Study dataset



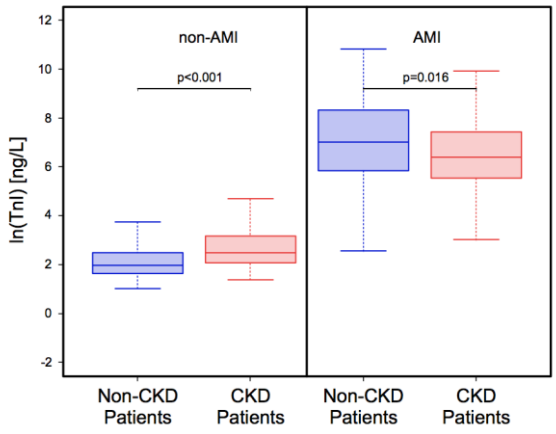
B) Clinical dataset



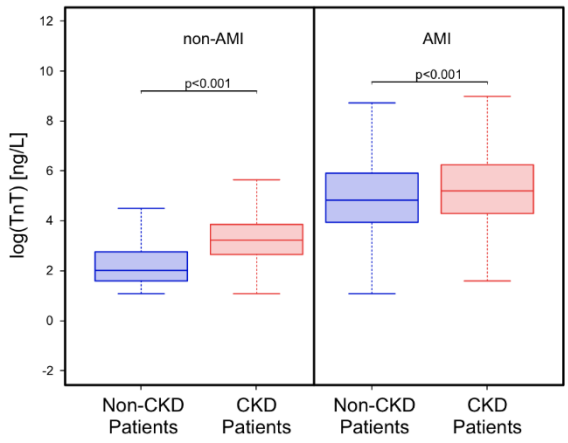
Sensitivity, specificity and sum of sensitivity and specificity of **(A)** hs-cTnI and **(B)** hs-cTnT determined upon admission in patients with acute chest pain and CKD to identify an acute myocardial infarction.

Figure S3. Second troponin measurements in patients with or without CKD and with or without NSTE-AMI

A) Study dataset



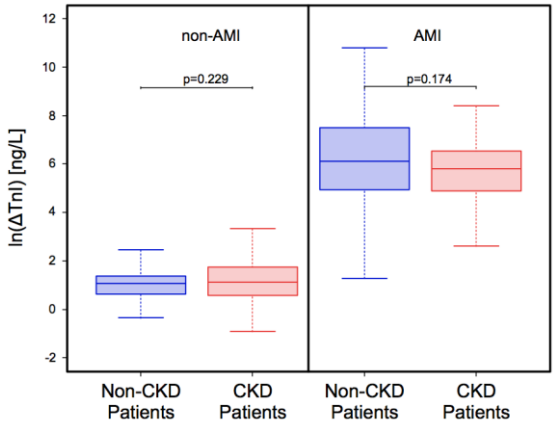
B) Clinical dataset



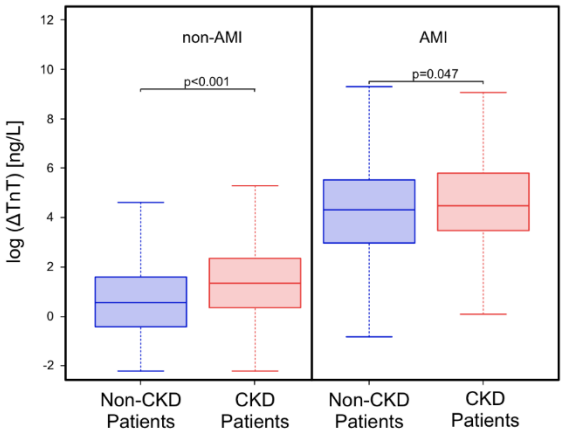
(A) hs-cTnI and **(B)** hs-cTnT levels three hours after admission in patients with acute chest pain according to renal function (eGFR, estimated glomerular filtration rate) and final diagnosis.

Figure S4. Serial differences in troponin levels in patients with or without CKD and with or without NSTE-AMI

A) Study dataset



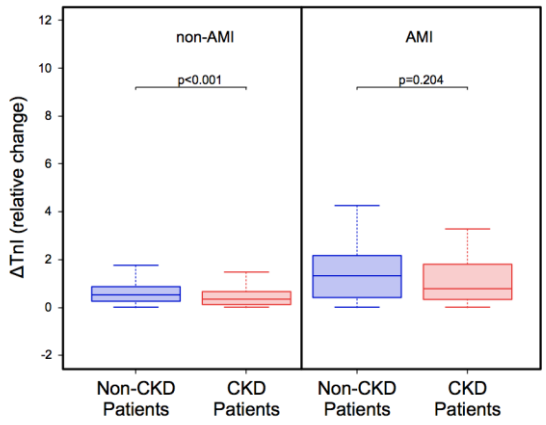
B) Clinical dataset



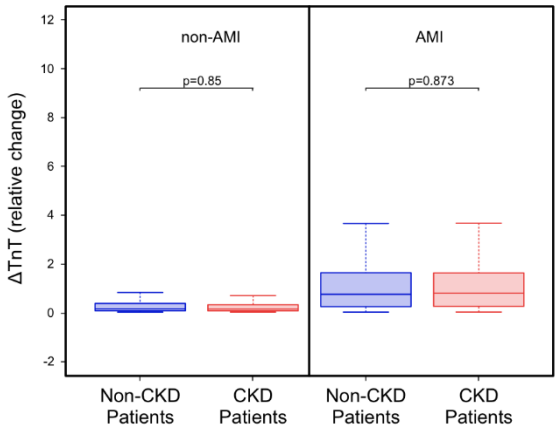
Differences between serial **(A)** hs-cTnI and **(B)** hs-cTnT measurements. Values are expressed in ng/L as median and interquartile ranges. Only cases with an increase in troponin levels after 3 hours were included in this analysis (1185 of 1494 cases in the study dataset and 1944 of 4478 cases in the clinical dataset).

Figure S5. Serial changes in troponin levels in patients with or without CKD and with or without NSTE-AMI

A) Study dataset



B) Clinical dataset



Relative changes of serial **(A)** hs-cTnI and **(B)** hs-cTnT measurements. Values are expressed in ng/L as median and interquartile ranges. Only cases with an increase in troponin levels after 3 hours were included in this analysis (1185 of 1494 cases in the study dataset and 1944 of 4478 cases in the clinical dataset).