Appendix 1 (as supplied by the authors): Online-only supplement

SUPPLEMENTAL METHODS

1) Use of local conventional cTn values for adjudication of final diagnoses

For the Roche cTnT 4th generation assay, the 10% CV level is 0.035ug/l. The laboratories of the participating sites reported only two decimals; therefore 0.04ug/l was used as a cut-off for myocardial necrosis. In order to fulfil the criteria of a significant change (30% of 99th percentile or 10% CV level), a patient would e.g. need to have a level of <0.01ug/l at presentation and 0.04ug/l at 6h. A patient would also qualify if the first level is 0.02ug/l and the second 0.04ug/l. A patient would not fulfil the criteria if the first level is 0.03ug/l and the second is 0.04ug/l. If the first level is 0.04ug/l, the second level needs to be at least 0.06ug/l.

For the Abbott AxsymcTnI ADV, the 10% CV level is 0.16ug/l. A patient having 0.16ug/l at presentation would meet the criteria for significant change if the second was ≥0.21ug/l. A patient having <0.12ug/l at presentation (limit of detection) would qualify if the second is >0.16ug/l.

For the Beckmann Coulter AccucTnI, the 10% CV level is 0.06ug/l. A patient having 0.06ug/l at presentation would qualify if the second is ≥0.08ug/l. A patient having 0.05 at presentation would qualify if the second is 0.07ug/l, but not 0.06ug/l. A patient having undetectable cTnI (cTnI<0.01ug/l) at presentation would qualify if the second is ≥0.06ug/l.

2) Use of hs-cTnT for adjudication of final diagnoses

In order to identify additional patients with small AMIs that were missed by the adjudication using the less sensitive conventional cTn assays a second adjudication

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using hs-cTnT was performed in all non-AMI patients according to the first adjudication. For hs-cTnTthe 99th percentile (14ng/l) was used as cut-off for myocardial necrosis.[1,2]

Absolute changes in hs-cTnT were used to determine significant changes based on the diagnostic superiority of absolute over relative changes [3,4]. Based on studies of the biological variation of cTn[5,6] as well as on data from previous chest pain cohort studies[7,8], a significant absolute change was defined as a rise or fall of at least 10ng/l within six hours. In patients, in whom a 6 hour hs-cTnT level was not available, changes were assessed at earlier time points. In an assumption of near-linearity, an absolute change of 6ng/l within three hours was considered.

3) Assumption of linearity of absolute changes within the first hours

The assumption of linearity of absolute changes within the first hours is based on unpublished internal data as well as recent data from Ola Hammarsten et al. showing a near-linear increase in levels of cTn with increasing time from symptom onset in their NSTEMI cohort. [9]

Calculation of the glomerular filtration rate was performed using the abbreviated Modification of Diet in Renal disease formula [10].

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SUPPLEMENTAL TABLES

Supplemental Table 1	Latest hs-cTnT value available x hours after presentation (all patients n=1320)	
	n	%
≥0h after presentation	1320	100
≥1h after presentation	1320	100
≥2h after presentation	1320	100
≥3h after presentation	1208	92
≥4h after presentation	851	64
≥5h after presentation	725	55
≥6h after presentation	695	53

Supplemental Table 2	Latest hs-cTnT value available x hours after presentation (all patients n=1320)	
	n	%
≥0h after presentation	1320	100
≥1h after presentation	1320	100
≥2h after presentation	1320	100
≥3h after presentation	1306	99
≥4h after presentation	1263	96
≥5h after presentation	1191	90
≥6h after presentation	1096	83

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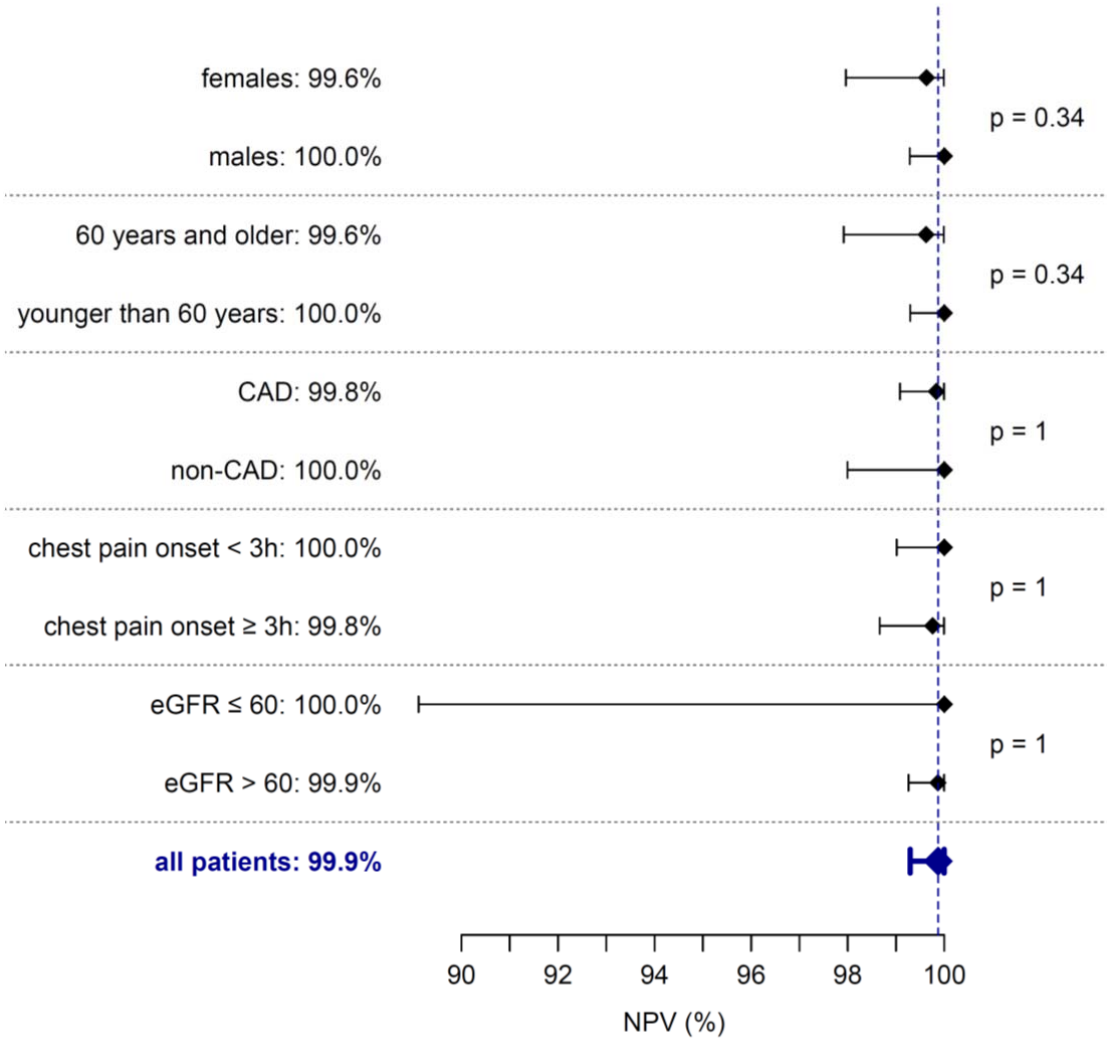
SUPPLEMENTAL FIGURE 1



Suppl Figure 1	**Forest plot indicating NPV of the 1h-algorithm in study subgroups**

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Supplemental Tables

Suppl Table 1	Baseline Characteristics of the Patients			
	All patients (n=1656)	**0h & 1h samples available** (n=1320)	**Samples incomplete** (n=336)	**P Value**
Age – yr	60 (49 – 74)	60 (49 – 73)	61 (47 – 76)	0.46
Male gender – no. (%)	1146 (69)	915 (69)	231 (69)	0.84
Risk factors – no. (%)				
Hypertension	972 (59)	770 (58)	202 (21)	0.55
Hypercholesterolemia	820 (50)	658 (50)	162 (48)	0.59
Diabetes	273 (17)	218 (17)	55 (16)	0.95
Current smoking	433 (26)	345 (26)	88 (26)	0.95
History of smoking	613 (37)	501 (38)	112 (34)	0.13
History – no. (%)				
Coronary artery disease	557 (34)	440 (33)	117 (35)	0.61
Previous myocardial infarction	388 (23)	305 (23)	83 (25)	0.54
Previous revascularization	465 (28)	372 (28)	93 (28)	0.86
Peripheral artery disease	93 (6)	71 (5)	22 (7)	0.41
Previous stroke	87 (5)	75 (6)	12 (4)	0.12
Creatinine clearance - (ml/min/m2)	85 (70 – 101)	85 (70 – 101)	83 (62 – 101)	0.19
Adjudicated final diagnosis				
Acute myocardial infarction	295 (18)	229 (17)	66 (20)	0.33
Unstable Angina	137 (8)	109 (8)	28 (8)	0.96
Cardiac but non coronary disease	234 (14)	194 (15)	40 (12)	0.26
Non-cardiac chest pain	920 (56)	732 (56)	188 (56)	0.87
Unknown	70 (4)	56 (4)	14 (4)	0.95

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