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Heart

SUPPLEMENTAL MATERIAL

Using Historical Cardiac Troponins to Identify Patients at a High Risk of Myocardial Infarction

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Supplemental Table 1. Combination of historical hs-cTnT concentrations and 0 h hs-cTnT with corresponding relative change and historical-adjusted 0 h hs-cTnT

Historical hs-cTnT (ng/l)	0 hs-cTnT (ng/l)	Relative change (%)	Historical-adjusted 0 h hs-cTnT
5	20	300	60.0
10	25	150	37.5
15	30	100	30.0
20	35	75	26.3
25	40	60	24.0
30	45	50	22.5
35	50	43	21.4
40	55	38	20.6
45	60	33	20.0
50	65	30	19.5
55	70	27	19.1
60	75	25	18.8
65	80	23	18.5
70	85	21	18.2
75	90	20	18.0
80	95	19	17.8
85	100	18	17.6
90	105	17	17.5
95	110	16	17.4
100	115	15	17.3

Abbreviations: hs-cTnT: high-sensitivity cardiac troponin T.

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Supplemental Table 2. Baseline characteristics according to tertiles of historical hs-cTnT-adjusted admission hs-cTnT

	Historical hs-cTnT-adjusted admission hs-cTnT		
	Lowest tertile	**Intermediate tertile**	**Highest tertile**
Number of visits	9132 (33)	9226 (33)	9451 (34)
Age (years), median (IQR)	68 (56-78)	72 (61-81)	76 (65-84)
Women	4087 (45)	4063 (44)	3922 (42)
Comorbidities			
Prior MI	2166 (24)	2412 (26)	3046 (32)
Prior revascularization	2406 (26)	2556 (28)	2816 (30)
Prior stroke	917 (10)	1112 (12)	1412 (15)
Heart failure	2297 (25)	2915 (32)	3713 (39)
Diabetes	2026 (22)	6793 (26)	2838 (30)
Hypertension	5570 (61)	6305 (68)	6838 (72)
Atrial fibrillation	2422 (27)	3057 (33)	3347 (35)
Dialysis	60 (0.7)	75 (0.8)	263 (2.8)
COPD	1180 (13)	1451 (16)	1590 (17)
Laboratory data			
First hs-cTnT concentration (ng/l), median (IQR)	9 (6-15)	13 (9-17)	25 (20-71)
Historical hs-cTnT concentration, (ng/l), median (IQR)	8 (4.9-13)	9 (5.4-17)	14 (7-29)
Relative change between historical and first hs-cTnT concentration, median (IQR)	11% (5-18)	33% (23-48)	108% (60-217)
Hemoglobin (g/l), median (IQR)	137 (127-148)	136 (124-147)	131 (118-143)
Nt-pro-BNP (ng/l), median (IQR)	519 (141-1730)	884 (268-2810)	2098 (624-5770)
eGFR (ml/min/1.73 m2):			
>60	7159 (78)	6357 (69)	5105 (54)
30-59	1766 (19)	2507 (27)	3184 (34)
<30	207 (2.3)	362 (3.9)	1162 (12)
Medications			
Aspirin	3534 (39)	3944 (43)	4403 (47)

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P2Y12 inhibitors*	1070 (12)	1039 (11)	1201 (13)
Any platelet inhibitor†	3940 (43)	4389 (48)	4909 (52)
Beta-blockers	4855 (53)	5415 (59)	5807 (61)
ACEi/ARB	4325 (47)	4800 (52)	5091 (54)
Statins	3754 (41)	4012 (43)	4133 (44)
OAC‡	1531 (17)	1890 (20)	7595 (20)
Warfarin	1207 (13)	1564 (17)	1507 (16)
DOAC	358 (3.9)	360 (3.9)	376 (4.0)

Data are presented as n (%), or median with IQR. *Includes treatment with Clopidogrel, Tikagrelor, Dipyradimol or Prasugel. †Includes treatment with Aspirin or P2Y12 inhibitors. ‡Includes treatment with DOAC or Warfarin. Abbreviations: ACEi/ARB: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; COPD: chronic obstructive pulmonary disease; hs-cTnT: high-sensitivity cardiac troponin T; eGFR: estimated glomerular filtration rate; MI: myocardial infarction; DOAC: direct oral anticoagulants; Nt-pro-BNP: N-terminal pro b-type natriuretic peptide; OAC: oral anticoagulants.

Supplemental Table 3. The most common discharge diagnoses according to tertiles of historical-adjusted 0 h hs-cTnT

	Historical-adjusted 0 h hs-cTnT		
	Lowest tertile	**Intermediate tertile**	**Highest tertile**
Discharge diagnoses			
#1 Diagnosis	Symptom diagnoses (R00-R09), 4147 (51)	Symptom diagnoses (R00-R09), 3712 (45)	Symptom diagnoses (R00-R09), 2314 (27)
#2 Diagnosis	AP (I20.9), 380 (4.7)	AP (I20.9), 431 (5.2)	MI (I21, I22), 1510 (18)
#3 Diagnosis	Unspecified pain, (M79), 302 (3.7)	HF, (I50), 361 (4.3)	AF (I48), 525 (6.2)
#4 Diagnosis	General symptoms and signs of illness (R50-R69), 247 (3.0)	Unspecified pain, (M79), 273 (3.3)	HF (I50), 525 (6.2)
#5 Diagnosis	Abdominal symptoms (R10-19), 232 (2.9)	General symptoms and signs of illness (R50-R69), 208 (2.5)	AP (I20.9), 382 (4.5)

Note: data are presented as proportions of patients among visits for which there was a final diagnosis available. Missing data within each tertile: 983 (11) (lowest), 916 (9.9) (intermediate), and 970 (10) (highest). Abbreviations: AP: angina pectoris; HF: heart failure; hs-cTnT: high-sensitivity cardiac troponin T; MI: myocardial infarction.

Supplemental Table 4. Patient characteristics in visits with a negative or 0 Δ hs-cTnT

	Visits with negative Δ hs-cTnT >20%		Visits with negative Δ hs-cTnT of 0 to 20%§	
	Visits with MI	**Visits without MI**	**Visits with MI**	**Visits without MI**
Number of visits	1350 (8.2)	15,191 (92)	404 (1.3)	31,154 (99)
Age (years), median (IQR)	75 (65-85)	69 (56-79)	74 (64-84)	57 (44-70)
Women	780 (58)	8578 (56)	251 (62)	15,003 (48)
Comorbidities				
Prior MI	1172 (87)	6410 (42)	276 (68)	5059 (16)
Prior revascularization	758 (56)	5822 (38)	209 (52)	5555 (18)
Prior stroke	200 (15)	1604 (11)	78 (19)	1971 (6.3)
Heart failure	544 (40)	4752 (31)	173 (43)	5183 (17)
Diabetes	505 (37)	3644 (24)	153 (38)	4810 (15)
Hypertension	1062 (79)	9865 (65)	320 (79)	13,078 (42)
Atrial fibrillation	407 (30)	4769 (31)	122 (30)	5760 (18)
Dialysis	43 (3.2)	232 (1.5)	12 (3.0)	185 (0.6)
COPD	145 (11)	1993 (13)	70 (17)	2700 (8.7)
Laboratory data				
First hs-cTnT concentration (ng/l), median (IQR)	31 (16-64)	10 (6-18)	22 (11-41)	4.9 (4.9-9)
Historical hs-cTnT concentration, (ng/l), median (IQR)	172 (58-570)	26 (12-85)	24 (12-46)	4.9 (4.9-10)
Relative change between historical and first hs-cTnT concentration, median (IQR)	-76 (-92, -48)	-46 (-79, -30)	-8 (-14, -2)	0 (-7.5, 0)
Hemoglobin (g/l), median (IQR)	129 (116-141)	135 (123-146)	130 (119-142)	137 (127-148)
Nt-pro-BNP (ng/l), median (IQR)	2580 (831-6670)	891 (248-2859)	1075 (247-3620)	369 (91-1520)
eGFR (ml/min/1.73 m2):				
>60	712 (53)	11,322 (75)	234 (58)	27,224 (87)
30-59	468 (35)	3242 (21)	120 (30)	3360 (11)
<30	170 (13)	627 (4.1)	50 (12)	570 (1.8)

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Medications

Aspirin	857 (63)	7001 (46)	257 (64)	8418 (27)
P2Y12 inhibitors*	403 (30)	2925 (19)	102 (25)	2552 (8.2)
Any platelet inhibitor†	924 (68)	7749 (51)	276 (68)	9350 (30)
Beta-blockers	944 (70)	9419 (62)	287 (71)	12,009 (39)
ACEi/ARB	832 (62)	8217 (54)	257 (64)	10,132 (33)
Statins	756 (56)	7036 (46)	234 (58)	8793 (28)
OAC‡	167 (12)	2763 (18)	59 (15)	3514 (11)
Warfarin	135 (10)	2155 (14)	48 (12)	2792 (9.0)
DOAC	38 (2.8)	669 (4.4)	12 (3.0)	814 (2.6)

Mortality within 30 days

All-cause mortality	78 (5.8)	179 (1.2)	24 (5.9)	137 (0.4)
Cardiovascular mortality	64 (4.7)	95 (0.6)	18 (4.5)	56 (0.2)
Non-cardiovascular mortality	14 (1.0)	84 (0.6)	6 (1.5)	81 (0.3)

Data are presented as n (%), or median with IQR. *Includes treatment with Clopidogrel, Tikagrelor, Dipyradimol or Prasugel. †Includes treatment with Aspirin or P2Y12 inhibitors. ‡Includes treatment with DOAC or Warfarin. §The interval of 0 to 20% was chosen as only a small proportion of patients had an exact Δhs-cTnT of zero. Abbreviations: ACEi/ARB: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; COPD: chronic obstructive pulmonary disease; hs-cTnT: high-sensitivity cardiac troponin T; eGFR: estimated glomerular filtration rate; MI: myocardial infarction; DOAC: direct oral anticoagulants; Nt-pro-BNP: N-terminal pro b-type natriuretic peptide; OAC: oral anticoagulants.

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Supplemental Table 5. Quantile regression predictors of historical high-sensitivity cardiac troponin T concentrations and Δ high-sensitivity cardiac troponin T

		Historical hs-cTnT		Δ hs-cTnT	
		Unadjusted model	**Adjusted model**	**Unadjusted model**	**Adjusted model**
		Parameter estimate of median hs-cTnT, ng/l (95% CI)		*Parameter estimate of Δ hs-cTnT (95% CI)*	
Age (years)					
	>84	19.9 (19.2-20.6)	13.6 (13.3-14.0)	34% (32-36)	38% (35-40)
	64-75	13.0 (12.9-13.0)	9.4 (9.1-9.6)	33% (33-34)	36% (34-37)
	76-84	9.0 (9.0-9.0)	7.0 (6.8-7.1)	33% (33-34)	36% (35-38)
	<64	5.9 (5.7-6.1)	5.3 (5.2-5.5)	30% (28-32)	33% (31-34)
Sex					
	Men	10.0 (10.0-10.0)	13.6 (13.3-14.0)	33% (33-34)	38% (35-40)
	Women	9.5 (9.1-9.8)	11.6 (11.3-11.9)	33% (33-34)	36% (34-38)
eGFR (mL/min/1.73m^2)					
	≥60	7.3 (7.0-7.6)	13.6 (13.3-14.0)	32% (31-34)	38% (35-40)
	30-60	16.0 (15.6-16.4)	17.3 (17.0-17.6)	33% (33-34)	41% (38-43)
	<30	34.1 (32.9-35.3)	34.2 (33.0-35.4)	43% (41-46)	51% (48-55)
Prior MI					
	No	9.0 (8.7-9.2)	13.6 (13.3-14.0)	33% (32-33)	38% (35-40)
	Yes	14.0 (13.6-14.4)	15.3 (15.0-15.6)	32% (30-33)	36% (34-38)
Prior heart failure					
	No	8.0 (7.9-8.1)	13.6 (13.3-13.9)	33% (33-34)	38% (36-40)
	Yes	18.0 (17.7-18.3)	17.4 (17.0-17.7)	30% (29-31)	33% (31-35)
Prior atrial fibrillation					
	No	8.0 (8.0-8.0)	13.6 (13.3-13.9)	33% (33-34)	38% (35-40)
	Yes	14.3 (13.7-15.0)	14.7 (14.4-15.0)	30% (29-31)	33% (31-36)

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Prior stroke

No	9.0 (8.8-9.2)	13.6 (13.3-13.9)	33% (33-34)	38% (36-40)
Yes	14.6 (13.9-15.3)	14.5 (14.0-14.9)	33% (32-35)	38% (36-41)

Prior diabetes

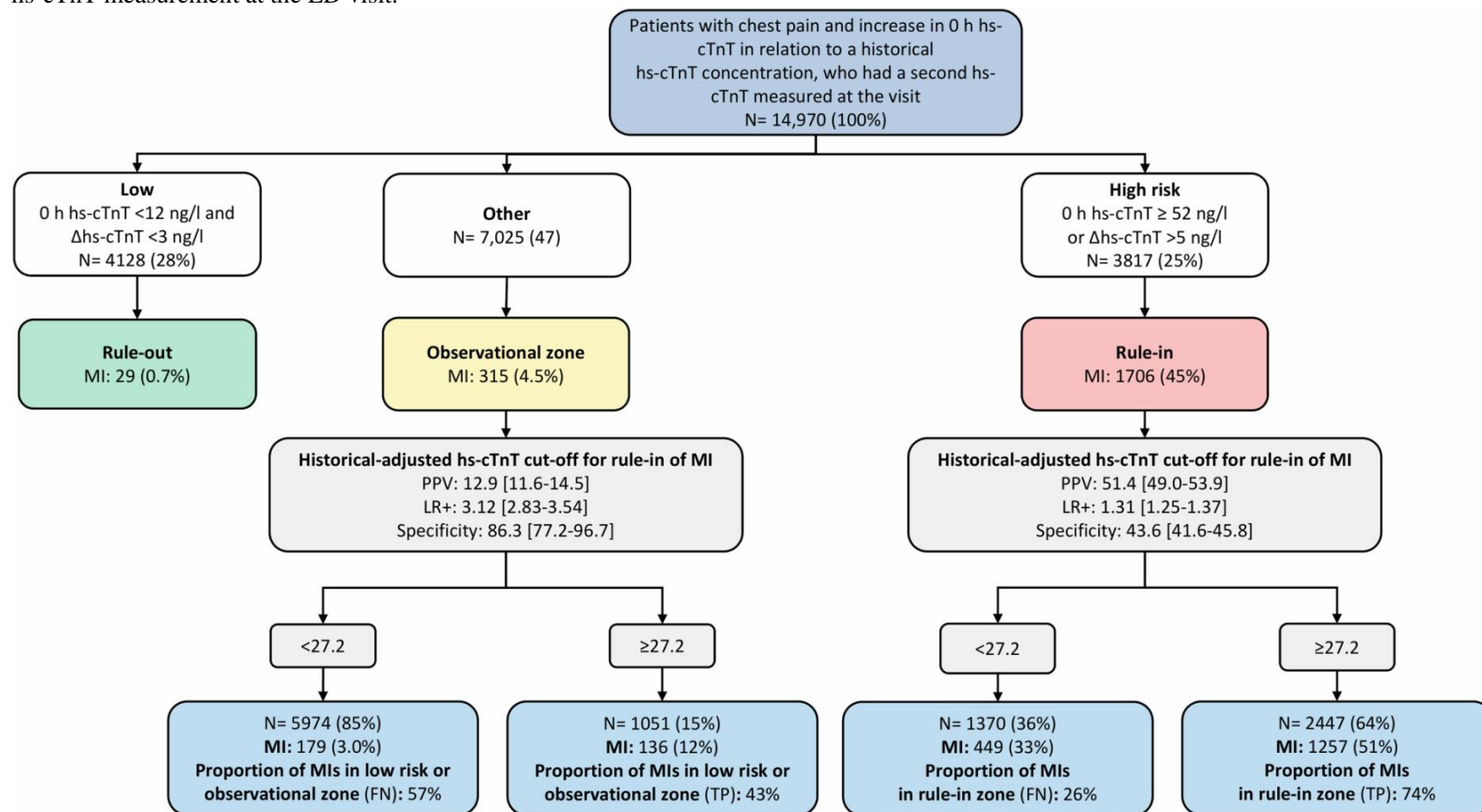|				
No	9.0 (8.9-9.1)	13.6 (13.3-13.9)	33% (33-34)	38% (35-40)
Yes	14.0 (13.4-14.6)	15.5 (15.1-15.9)	33% (32-34)	37% (35-40)

Prior COPD

No	9.0 (9.0-9.1)	13.6 (13.3-13.9)	33% (33-34)	38% (36-40)
Yes	14.0 (13.3-14.7)	15.3 (14.9-15.6)	32% (30-34)	38% (35-40)

Abbreviations: COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; hs-cTnT: high-sensitivity cardiac troponin T; eGFR: estimated glomerular filtration rate.

Supplemental Figure 1. Diagnostic performance of historical-adjusted hs-cTnT for diagnosing myocardial infarction in patients with a second hs-cTnT measurement at the ED visit.

Note: No patients had a very low risk according to the 0 h hs-cTnT (i.e. a 0 h hs-cTnT <5 ng/l), as only patients with a positive historical Δhs-cTnT were included. The Δhs-cTnT concentration in the figure refers to the hs-cTnT change between the 0 h hs-cTnT and the second hs-cTnT measurement. Abbreviations: FN: false negative; Hs-cTnT: high-sensitivity cardiac troponin T; MI: myocardial infarction; LR+: positive likelihood ratio, PPV: positive predictive value; TP; true positive.