

ONLINE SUPPLEMENTARY APPENDIX

To the manuscript

Comparison of a single high-sensitivity cardiac Troponin T measurement with the HEART score for rapid rule-out of acute myocardial infarction in a primary care emergency setting: a cohort study

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ONLINE TABLE 1 Selection of patients with chest pain or other symptoms suggestive of NSTEMI-ACS at the OAEOC

GP triage	NSTEMI-ACS not suspected = Other causes/disorders more likely	NSTEMI-ACS mild to moderately suspected = In need of further tests to rule-out AMI without urgent need of hospitalisation	NSTEMI-ACS or STEMI highly suspected = In need of urgent hospitalisation for more advanced testing/care
Examples	<ul style="list-style-type: none"> • Myalgia • Costochondritis • Tietze's syndrome • Stress • Anxiety • Panic disorder • Pulmonary infection • COPD • Pulmonary embolism • Gastric reflux • Gastritis • Gastric ulcer • Cholelithiasis • Acute pancreatitis 	<ul style="list-style-type: none"> • Pain-free but mild to moderately suspected history/clinical presentation • Patients without classic cardiac chest pain, but concomitant symptoms of unknown origin consistent with possible CAD (e.g. single syncope, acute dyspnoea or acute fatigue) • Including the elderly, diabetics, and patients with several comorbidities 	<ul style="list-style-type: none"> • History/clinical presentation highly suspicious <i>And/or</i> <ul style="list-style-type: none"> • Ongoing or recurrent cardiac-suspected chest pain <i>And/or</i> <ul style="list-style-type: none"> • Ischaemic suspected ECG (including significant ST-segment elevation/depression or new LBBB) <i>And/or</i> <ul style="list-style-type: none"> • Haemodynamic instability <i>And/or</i> <ul style="list-style-type: none"> • Respiratory distress
Further management	Home with/without treatment OR hospitalised due to other conditions	Admission at the OAEOCs observation unit for serial hs-cTnT measurements in order to rule-out AMI	Direct transfer to hospital by ambulance (usually within 20-60 minutes after OAEOC arrival)

AMI: acute myocardial infarction; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; ECG: electrocardiogram; GP: general practitioner; hs-cTnT: high-sensitivity cardiac troponin T; NSTEMI-ACS: non-ST-segment elevation acute coronary syndrome; OAEOC: Oslo Accident and Emergency Outpatient Clinic; STEMI: ST-segment elevation myocardial infarction

ONLINE TABLE 2 Details in the predefined study form

Basics	<ul style="list-style-type: none"> • Norwegian personal identity number (later replaced by a study ID) • Sex and Age
Time variables (time/date)	<ul style="list-style-type: none"> • Onset of symptoms • Arrival at the OAEOC • Admission at the OAEOC observation unit • Hs-cTnT measurements • OAEOC discharge
Risk factors for cardiovascular disease	<ul style="list-style-type: none"> • Current or history of smoking last ten years • Diabetes mellitus • Chronic obstructive pulmonary disease • Previous history of CAD • Hypertension • Hypercholesterolemia • Other CVD (valvular disease, previous cerebral stroke, cardiomyopathies, atrial fibrillation other arrhythmias), • History of CAD in first-degree sibling <60 years of age
Presenting acute symptoms	<ul style="list-style-type: none"> • Chest pain <ul style="list-style-type: none"> ○ Constricting ○ Tearing ○ Burning ○ Sharp ○ Respiratory-dependent ○ Position-dependent ○ Palpation-dependent • Pain radiation (arms, neck, jaws, upper abdomen, scapulae) • Acute dyspnoea • Acute fatigue • Syncope, pre-syncope • Observed or reported diaphoresis • Nausea or vomiting • Palpitations • Other pain: upper abdomen or upper back/scapulae only • No pain
ICD-10 discharge codes	<ul style="list-style-type: none"> • Given by GP responsible for OAEOC discharge
Further disposition after OAEOC discharge	<ul style="list-style-type: none"> • Home/no follow-up • Advised to contact regular GP • Referral to hospital outpatient clinic • Admitted at a municipality (primary care) short term facility • Left during observation • Admitted hospital • Direct transfer to the cath lab

CAD: coronary artery disease; CVD: cardiovascular disease; GP: general practitioner; hs-cTnT: high-sensitivity cardiac troponin T; ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th Revision; OAEOC: Oslo Accident and Emergency Outpatient Clinic

Laboratory analysis

Venous blood samples were collected in serum tubes and stored locally at room temperature (approximately 20 °C) for a maximum of 30 minutes before centrifugation, then stored in a refrigerator before being sent to the laboratory every four hours, as per standard procedure at the primary care emergency clinic. Hs-cTnT was analysed at the Department of Medical Biochemistry at Oslo University Hospital Ullevaal on the Cobas 8000 e602 and later the Cobas 8000 e801 Module Analyzer using the Elecsys Troponin T hs STAT assay (Roche Diagnostics, Switzerland). The cTnT has a stability of 24 hours with storage at 2-8 °C,^[1,2] and similar stability has previously been demonstrated for hs-cTnT samples stored under the conditions in our study.^[3] EQA (external quality assessment) material from Noklus (Bergen, Norway) and Equalis (Equalis AB, Uppsala, Sweden) was regularly analysed at the central lab with good performance during the inclusion period. The coefficient of variation (CV) was 6 % at concentrations ≥ 20 ng/L and 10 % at concentrations < 20 ng/L.

ONLINE TABLE 3 The History component of the HEART score used in the OUT-ACS study

Non-typical elements for ACS	Typical elements for ACS
<ul style="list-style-type: none"> • Sharp or burning chest pain • Pain in the upper abdomen or upper back/scapulae only • Palpation, position or respiratory-dependent pain • Acute fatigue • Syncope/pre-syncope • Palpitations 	<ul style="list-style-type: none"> • Constricting or tearing retrosternal chest pain • Radiation of pain to arms, neck or jaws • Diaphoresis (observed or reported) • Vomiting, nausea • Acute dyspnoea

Following the original HEART score,^[4] the History is considered highly suspicious and given 2 points if only typical elements are reported, 1 point if the medical history contains a combination of both non-typical and typical elements, and 0 points if all elements in are considered non-typical.

The following classification of which elements are considered non-suspicious or suspicious are defined by the OUT-ACS study investigators in this table, based on symptoms reported at the initial examination.

ACS: acute coronary syndrome; HEART: History, ECG, Age, Risk factors and Troponin; OAEOC: Oslo Accident and Emergency Outpatient Clinic

ONLINE TABLE 4 Separate 2x2-tables used in the calculation of the diagnostic performance for the three different strategies

	Single hs-cTnT		Original HEART score		Modified HEART score	
	Rule-out group	Rule-in group	Low-risk group	High-risk group	Low-risk group	High-risk group
True positive	61	34	56	18	60	21
False positive	1081	10	784	62	1012	175
False negative	0	27	5	43	1	40
True negative	569	1640	866	1588	638	1475
Total	1711	1711	1711	1711	1711	1711

The diagnostic performance for each rule-out, rule-in, low-risk, and high-risk groups were calculated separately.

HEART: History, ECG, Age, Risk factors and Troponin; hs-cTnT: high-sensitivity cardiac troponin T

ONLINE TABLE 5 Disposition after ended observation at the OAEOC									
n (%)	Single hs-cTnT			Original HEART score			Modified HEART score		
	Rule out	Observation	Rule in	Low risk	Inter-mediate	High risk	Low risk	Inter-mediate	High risk
No follow-up	163 (28.6)	230 (20.9)	1 (2.3)	247 (28.4)	141 (18.6)	6 (7.5)	190 (29.7)	180 (20.5)	24 (12.2)
Contact regular GP	344 (60.5)	631 (57.5)	1 (2.3)	513 (58.9)	431 (56.7)	32 (40.0)	374 (58.5)	512 (58.4)	90 (45.9)
Admitted municipal short term facility	0 (0.0)	21 (1.9)	2 (4.5)	2 (0.2)	17 (2.2)	4 (5.0)	2 (0.3)	16 (1.8)	5 (2.6)
Referral to hospital outpatient clinic	20 (3.5)	47 (4.3)	0 (0.0)	27 (3.1)	35 (4.6)	5 (6.3)	20 (3.1)	31 (3.5)	16 (8.2)
Left during observation	10 (1.8)	15 (1.4)	0 (0.0)	16 (1.8)	9 (1.2)	0 (0.0)	13 (2.0)	12 (1.4)	0 (0.0)
Admitted hospital	32 (5.6)	153 (13.9)	37 (84.1)	66 (7.6)	124 (16.3)	32 (40.0)	40 (6.3)	122 (13.9)	60 (30.6)
Direct coronary angiography	0 (0.0)	1 (0.1)	3 (6.8)	0 (0.0)	3 (0.4)	1 (1.3)	0 (0.0)	3 (0.3)	1 (0.5)
Total N = 1711	569 (33.3)	1098 (64.2)	44 (2.6)	871 (50.9)	760 (44.4)	80 (4.7)	639 (37.3)	125 (51.2)	196 (11.5)

GP: general practitioner; HEART: History, ECG, Age, Risk factors, Troponin; hs-cTnT: high-sensitivity cardiac troponin T; OAEOC: Oslo Accident and Emergency Outpatient Clinic

ONLINE TABLE 6 Misclassification in the original low-risk HEART score group

Sex	Age	HEART score	Symptom onset to first hs-cTnT, hours	hs-cTnT at the OAEOC			Disposition after OAEOC	Adjudicated final diagnosis
				0-hour	1-hour	4-hour		
Female	40	3	1.8	30	69	X	Hospital	AMI
Male	59	3	2.3	9	12	37	Hospital	AMI
Female	57	3	5.7	13	X	X	Hospital	AMI
Male*	32	3	9.5	378	481	X	Hospital	AMI
Female	70	3	18.1	5	6	13	Home	AMI

*Also misclassified by the modified low-risk HEART score.

AMI: acute myocardial infarction; HEART: History, ECG, Age, Risk factors and Troponin; hs-cTnT: high-sensitivity cardiac troponin T; OAEOC: Oslo Accident and Emergency Outpatient Clinic; X: not measured due to hospitalisation

ONLINE TABLE 7 Classification of the HEART scores compared to single hs-cTnT approach and the 0/1-hour algorithm for hs-cTnT

			Original HEART score		Modified HEART score	
			n	%	n	%
Single hs-cTnT (n=1711)	Rule-out (n=569)	Low risk	430	75.6	430	75.6
		Intermediate	138	24.3	138	24.3
		High risk	1	0.2	1	0.2
	Observation (n=1098)	Low risk	440	40.1	208	18.9
		Intermediate	595	54.2	711	64.8
		High risk	63	5.7	179	16.3
	Rule-in (n=44)	Low risk	1	2.3	1	2.3
		Intermediate	27	61.4	27	61.4
		High risk	16	36.4	16	36.4
0/1-hour algorithm (n=1711)^[5]	Rule-out (n=1311)	Low risk	815	62.2	617	47.1
		Intermediate	490	37.4	658	50.2
		High risk	6	0.5	36	2.7
	Observation (n=334)	Low risk	50	15.0	19	5.7
		Intermediate	231	69.2	178	53.3
		High risk	53	15.9	137	41.0
	Rule-in (n=66)	Low risk	6	9.1	3	4.5
		Intermediate	39	59.1	40	60.6
		High risk	21	31.8	23	34.8

The total HEART scores were stratified into three risk groups; low-risk (0-3 points), intermediate-risk (4-6 points), and high-risk (7-10 points), and further classified according to the single hs-cTnT strategy and the ESC 0/1-hour algorithm.

ESC: European Society of Cardiology; HEART: History, ECG, Age, Risk factors and Troponin; hs-cTnT: high-sensitivity cardiac troponin T

ONLINE TABLE 8 Distribution of the calculated HEART scores

Classification	Points	Original HEART score		Modified HEART score	
		n	%	n	%
Low risk	0	4	0.2	3	0.2
	1	110	6.4	74	4.3
	2	305	17.8	239	14.0
	3	452	26.4	323	18.9
Intermediate risk	4	377	22.0	350	20.5
	5	242	14.1	302	17.7
	6	141	8.2	224	13.1
High risk	7	60	3.5	130	7.6
	8	16	0.9	53	3.1
	9	4	0.2	13	0.8
	10	0	0.0	0	0.0
Total		1711	100.0	1711	100.0
Mean (SD)		3.64 (1.568)		4.22 (1.785)	

SD: standard deviation; HEART: History, ECG; Age; Risk factors; Troponin

References

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2. Giannitsis E, Kurz K, Hallermayer K, et al. Analytical validation of a high-sensitivity cardiac troponin T assay. *Clin Chem* 2010;56(2):254-61.
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4. Six AJ, Backus BE, Kelder JC. Chest pain in the emergency room: value of the HEART score. *Neth Heart J* 2008;16(6):191-6.
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