SUPPLEMENTAL MATERIAL

Use of Historical High-Sensitivity Cardiac Troponin T Levels to Rule Out Myocardial Infarction

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Roos A, Holzmann MJ. *Open Heart* 2022; 8:e001682. doi: 10.1136/openhrt-2021-001682

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Supplemental Table 1. Details of the selection of the study population

	Hospitals included in the study									
	Danderyd Hospital	KS-Solna	KS-Huddinge	St. Görans Hospital	SÖS	Södertälje Hospital	Sahlgrenska University Hospital	Östra Hospital	Mölndal Hospital	**Total number**
Location, city	Stockholm	Stockholm	Stockholm	Stockholm	Stockholm	Stockholm	Gothenburg	Gothenburg	Gothenburg	
Number of visits for chest pain in patients ≥35 years of age	32,185	15,705	22,025	25,614	37,233	8,267	19,371	17,961	8,260	186,621
Patients with STEMI	355	151	224	255	471	90	167	167	87	1,967
Number of visits for chest pain with hs-cTnT measurement	28,821	14,360	20,191	14,466	33,446	5,137	18,108	15,232	6,432	156,193
Patients with a 0-h hs-cTnT level and a second hs-cTnT value measured between 45 min to ≤3.5 h	7,109	4,910	2,549	1,595	4,527	276	8,606	6,954	1,964	38,490
Patients with a 0-h hs-cTnT <12 ng/l	4,690	3,210	1,412	1,072	2,735	189	4,909	3,219	847	22,283
Patients with ≥1 historical hs-cTnT level available from a previous visit for any reason	1,739	1,315	637	384	1,046	67	1,799	1,166	279	8,432

Abbreviations: Hs-cTnT: high-sensitivity cardiac troponin t; KS-Huddinge: Karolinska University Hospital, Huddinge; KS-Solna: Karolinska University Hospital, Solna; STEMI: ST-segment elevation myocardial infarction; SÖS: Stockholm South General Hospital.

Supplemental Table 2. Incidence of myocardial infarction

			Historical hs-cTnT concentration			
		Delta hs-cTnT*	>12 ng/l any	<12 ng/l <3 ng/l	<12 ng/l >3 ng/l	**Total**
Delta hs-TnT†	<3 ng/l	MI ≤30 days, n	10/1202	19/6503	6/395	35/8100
		30-day MI risk (95% CI)	0.8% (0.4–1.6)	0.3% (0.2–0.5)	1.5% (0.6–3.4)	0.4% (0.3–0.6)
	>3 ng/l	MI ≤30 days, n	18/92	17/197	14/43	49/332
		30-day MI risk (95% CI)	19.6% (12.3–29.4)	8.6% (5.3–13.7)	32.6% (19.5–48.7)	14.8% (11.2–19.1)
	Total	MI ≤30 days, n	28/1294	36/6700	20/438	84/8432
		30-day MI risk (95% CI)	2.2% (1.5–3.2)	0.5% (0.4–0.8)	4.6% (2.9–7.1)	1.0% (0.8–1.2)

*Change between the historical hs-cTnT and 0-h hs-cTnT level. †Change between the 0-h hs-cTnT and second hs-cTnT level. The **green** and yellow colours represent triage toward rule-out using the modified ESC algorithm and the historical-hs-cTnT algorithm, respectively. Abbreviation: hs-cTnT: high-sensitivity cardiac troponin t.

Supplemental Table 3. Performance of a modified ESC algorithm and a historical-hs-cTnT algorithm with the use of a historical hs-cTnT value as the 0-h value to rule out myocardial infarction and for the prediction of all-cause mortality, stratified by sex

	Men	**Women**
Number of eligible patients	4,269	4,163
MI ≤30 days after the index visit, n (%)	55 (1.3)	29 (0.7)
Algorithm using hs-cTnT measured at the same visit (modified ESC algorithm) Myocardial infarction		
Rule-out		
Number of patients ruled-out, n (%)	4,109 (96)	3,991 (96)
30-day risk of MI (95 CI%)	0.6% (0.4–0.9)	0.3% (0.1–0.5)
NPV, % (95 CI%)	99.4 (99.1–99.6)	99.7 (99.5–99.9)
LR^- (95 CI%)	0.47 (0.23-0.61)	0.36 (0.09-0.56)
Sensitivity, % (95 CI%)	54.5 (40.7–67.8)	65.5 (45.7–81.4)
Algorithm using a historical hs-cTnT value as the 0-h hs-cTnT value (historical-hs-cTnT algorithm) Myocardial infarction		
Rule-out		
Number of patients ruled-out, n (%)	3,270 (77)	3,430 (82)
30-day risk of MI (95 CI%)	0.9% (0.6–1.3)	0.2% (0.1–0.5)
NPV, % (95 CI%)	99.1 (98.7–99.4)	99.8 (99.5–99.9)
LR^- (95 CI%)	0.66 (0.35-1.00)	0.33 (0.09-0.57)
Sensitivity, % (95 CI%)	49.1 (35.5-62.8)	72.4 (52.5-86.6)
Algorithm using hs-cTnT measured at the same visit (modified ESC algorithm) All-cause mortality		
Rule-out		
30-day risk of all-cause mortality (95% CI)	0.1% (0.0–0.2)	0.2% (0.1–0.4)
NPV, % (95% CI)	99.9 (99.8–100)	99.8 (99.6–99.9)
LR^- (95% CI)	1.04 (0.08-1.06)	0.94 (0.23-1.04)
Sensitivity, % (95 CI%)	0 (0.0–69.0)	10.0 (0.5–45.9)
Algorithm using a historical hs-cTnT value as the 0-h hs-cTnT value (historical-hs-cTnT algorithm) All-cause mortality		
Rule-out		
30-day risk of all-cause mortality (95% CI)	0% (0.0–0.2)	0.1% (0.0–0.3)
NPV, % (95% CI)	100 (99.8–100)	99.9 (99.7–100)
LR^- (95% CI)	0.44 (0.01-1.22)	0.36 (0.03-1.00)
Sensitivity (95% CI)	66.7 (12.5-98.2)	70.0 (35.4-91.9)

Abbreviations: CI: confidence interval; hs-cTnT: high-sensitivity cardiac troponin t; LR−: negative likelihood ratio; MI: myocardial infarction; NPV: negative predictive value.

Supplemental Table 4. All-cause mortality

			Historical hs-cTnT concentration			
		Delta hs-cTnT*	>12 ng/l	<12 ng/l		**Total**
			any	<3 ng/l	>3 ng/l	
Delta hs-TnT†	<3 ng/l	Death ≤30 days, n	5/1202	4/6503	3/395	12/8100
		30-day all-cause mortality risk (95% CI)	0.4% (0.2–1.0)	0.1% (0.0–0.2)	0.8% (0.2–2.4)	0.1% (0.1–0.3)
	>3 ng/l	Death ≤30 days, n	1/92	0/197	0/43	1/332
		30-day all-cause mortality risk (95% CI)	1.1% (0.1–6.8)	0% (0.0–2.4)	0% (0.0–10.2)	0.3% (0.0–1.9)
	Total	MI ≤30 days, n	6/1294	4/6700	3/438	13/8432
		30-day all-cause mortality risk (95% CI)	0.5% (0.2–1.1)	0.1% (0.0–0.2)	0.7% (0.2–2.2)	0.2% (0.1–0.3)

*Change between the historical hs-cTnT and 0-h hs-cTnT level. †Change between the 0-h hs-cTnT and second hs-cTnT level. The **green** and yellow colours represent triage toward rule-out using the modified ESC algorithm and the historical-hs-cTnT algorithm, respectively. Abbreviation: hs-cTnT: high-sensitivity cardiac troponin t.

Supplemental Table 5. Performance of a modified ESC algorithm and a historical-hs-cTnT algorithm for rule out of myocardial infarction, stratified according to period of time before the remeasurement of hs-cTnT concentration

Algorithm using hs-cTnT measured at the same visit (modified ESC algorithm) **Early resampling group: second hs-cTnT concentration measured between 45 min and <2 h after the 0-h hs-cTnT concentration**			
	All patients	**Men**	**Women**
Number of eligible patients	3,847	1,932	1,915
MI ≤30 days after the index visit, n (%)	26 (0.7)	20 (1.0)	6 (0.3)
Rule-out			
Number of patients ruled-out, n (%)	3,734 (97)	1,870 (97)	1,864 (97)
30-day risk of MI (95% CI)	0.3% (0.1–0.5)	0.4% (0.2–0.9)	0.1% (0.0–0.4)
NPV, % (95% CI)	99.7 (99.5–99.9)	99.6 (99.1–99.8)	99.9 (99.6–100.0)
Sensitivity, % (95% CI)	61.5 (40.7–79.1)	60.0 (36.4–80.0)	66.7 (24.1–94.0)
Algorithm using hs-cTnT measured at the same visit (modified ESC algorithm) **Late resampling group: second hs-cTnT concentration measured between 2 h and ≤3.5 h after the 0-h hs-cTnT concentration**			
	All patients	**Men**	**Women**
Number of eligible patients	4,585	2,337	2,248
MI ≤30 days after the index visit, n (%)	58 (1.3)	35 (1.5)	23 (1.0)
Rule-out			
Number of patients ruled-out, n (%)	4,366 (95)	2,239 (96)	2,127 (95)
30-day risk of MI (95% CI)	0.6% (0.4–0.9)	0.8% (0.5–1.2)	0.4% (0.2–0.8)
NPV, % (95% CI)	99.4 (99.1–99.6)	99.2 (98.8–99.5)	99.6 (99.2–99.8)
Sensitivity, % (95% CI)	56.9 (43.3–69.6)	51.4 (34.3–68.3)	65.2 (42.8–82.8)
Algorithm using historical hs-cTnT concentration as the 0-h hs-cTnT concentration (historical-hs-cTnT algorithm) **Historical values measured at various times before the 0-h hs-cTnT concentration**			
	≤365 days before 0-h hs-cTnT		**>365 days before 0-h hs-cTnT**
Number of eligible patients	5,490		2,942
MI ≤30 days after the index visit, n (%)	54 (1.0)		30 (1.0)
Rule-out			
Number of patients ruled-out, n (%)	4,325 (94)		2,375 (93)
30-day risk of MI, (95% CI)	0.4% (0.3–0.7)		0.8% (0.5–1.2)
NPV, % (95% CI)	99.6 (99.3–99.7)		99.2 (98.8–99.5)
Sensitivity, % (95% CI)	66.7 (52.4-78.5)		40.0 (23.2-59.2)

Abbreviations: CI: confidence interval; hs-cTnT: high-sensitivity cardiac troponin t; MI: myocardial infarction; NPV: negative predictive value.

Supplemental Table 6. Performances of a modified ESC algorithm and a historical-hs-cTnT algorithm for the prediction of all-cause mortality, stratified according to the period of time to remeasurement of the hs-cTnT concentration

Algorithm using hs-cTnT measured at the same visit (modified ESC algorithm) **Early resampling group: second hs-cTnT concentration measured between 45 min and <2 h after the 0-h hs-cTnT concentration**			
	All patients	**Men**	**Women**
Number of eligible patients	3,847	1,932	1,915
Death ≤30 days after the index visit, n (%)	5 (0.1)	2 (0.1)	3 (0.2)
Rule-out			
30-day risk of all-cause mortality (95% CI)	0.1% (0.0–0.3)	0.1% (0.0–0.4)	0.2% (0.0–0.5)
NPV, % (95% CI)	99.9 (99.7–100.0)	99.9 (99.6–100.0)	99.8 (99.5–100.0)
Sensitivity, % (95% CI)	0.0 (0.0–53.7)	0.0 (0.0–80.2)	0.0 (0.0–69.0)
Algorithm using hs-cTnT measured at the same visit (modified ESC algorithm) **Late resampling group: second hs-cTnT concentration measured between 2 h and ≤3.5 h after the 0-h hs-cTnT concentration**			
	All patients	**Men**	**Women**
Number of eligible patients	4,585	2,337	2,248
Death ≤30 days after the index visit, n (%)	8 (0.2)	1 (0.0)	7 (0.3)
Rule-out			
30-day risk of all-cause mortality (95% CI)	0.2% (0.1–0.3)	0.0% (0.0–0.3)	0.3% (0.1–0.6)
NPV, % (95% CI)	99.8 (99.7–99.9)	100.0 (99.7–100.0)	99.7 (99.4–99.9)
Sensitivity, % (95% CI)	12.5 (0.7–53.3)	0.0 (0.0–94.5)	14.3 (0.8–58.0)
Algorithm using a historical hs-cTnT value as the 0-h hs-cTnT value (historical-hs-cTnT algorithm) **Historical values measured at various times before the 0-h hs-cTnT concentration**			
	≤365 days before the admission hs-cTnT measurement		**>365 days before the admission hs-cTnT measurement**
Number of eligible patients	5,490		2,942
Death ≤30 days after the index visit, n (%)	11 (0.2)		2 (0.1)
Rule-out			
30-day risk of all-cause mortality (95% CI)	0.1% (0.0–0.2)		0.0% (0.0–0.3)
NPV, % (95% CI)	99.9 (99.8–100.0)		100.0 (99.7–100.0)
Sensitivity, % (95% CI)	72.7 (39.3-92.7)		50.0 (2.7-97.3)

Abbreviations: CI: confidence interval; hs-cTnT: high-sensitivity cardiac troponin t; NPV: negative predictive value.

Supplemental Table 7. Performance of a historical-hs-cTnT algorithm for rule out of myocardial infarction and prediction of all-cause mortality, including patients with only one hs-cTnT concentration measured during the visit

Algorithm using a historical hs-cTnT value as the 0-h hs-cTnT value (historical-hs-cTnT algorithm) **Myocardial infarction**			
	All patients	**Men**	**Women**
Number of eligible patients	34,560	16,939	17,621
MI ≤30 days after the index visit, n (%)	252 (0.7)	163 (1.0)	89 (0.5)
Rule-out			
Number of patients ruled-out, n (%)	28,393 (82)	13,486 (80)	14,907 (85)
30-day risk of MI (95% CI)	0.4 (0.4-0.5)	0.6 (0.5-0.8)	0.3 (0.2-0.4)
NPV, % (95% CI)	99.6 (99.5-99.6)	99.4 (99.2-99.5)	99.7 (99.6-99.8)
Sensitivity, % (95% CI)	51.2 (44.9-57.5)	48.5 (40.6-56.4)	56.2 (45.3-66.5)

Algorithm using a historical hs-cTnT value as the 0-h hs-cTnT value (historical-hs-cTnT algorithm) **Myocardial infarction** **Historical values measured at various times before the 0-h hs-cTnT concentration**		
	≤365 days before the admission hs-cTnT measurement	**>365 days before the admission hs-cTnT measurement**
Number of eligible patients	24,527	10,033
MI ≤30 days after the index visit, n (%)	186 (0.8)	66 (0.7)
Rule-out		
Number of patients ruled-out, n (%)	20,022 (82)	8,371 (83)
30-day risk of MI (95% CI)	0.4 (0.3-0.5)	0.5 (0.3-0.7)
NPV, % (95% CI)	99.6 (99.5-99.7)	99.5 (99.3-99.7)
Sensitivity, % (95% CI)	55.4 (47.9-62.6)	39.4 (27.8-52.2)

Algorithm using a historical hs-cTnT value as the 0-h hs-cTnT value (historical-hs-cTnT algorithm) **All-cause mortality**			
	All patients	**Men**	**Women**
Number of eligible patients	34,560	16,939	17,621
Death ≤30 days after the index visit, n (%)	64 (0.2)	24 (0.1)	40 (0.2)
Rule-out			
30-day risk of all-cause mortality (95% CI)	0.2% (0.1-0.2)	0.1% (0.1-0.2)	0.2% (0.1-0.3)
NPV, % (95% CI)	99.8 (99.8-99.9)	99.9 (99.8-99.9)	99.8 (99.7-99.9)
Sensitivity, % (95% CI)	29.7 (19.2-42.6)	25.0 (10.6-47.1)	32.5 (19.1-49.2)

Algorithm using a historical hs-cTnT value as the 0-h hs-cTnT value (historical-hs-cTnT algorithm) **All-cause mortality** **Historical values measured at various times before the 0-h hs-cTnT concentration**

	≤365 days before the admission hs-cTnT measurement	**>365 days before the admission hs-cTnT measurement**
Number of eligible patients	24,527	10,033
Death ≤30 days after the index visit, n (%)	49 (0.2)	15 (0.1)
Rule-out		
30-day risk of all-cause mortality (95% CI)	0.2 (0.1-0.2)	0.1 (0.1-0.3)
NPV, % (95% CI)	99.8 (99.8-99.9)	99.9 (99.7-99.9)
Sensitivity, % (95% CI)	32.7 (20.4-47.7)	20.0 (5.3-48.6)

Abbreviations: CI: confidence interval; hs-cTnT: high-sensitivity cardiac troponin t; NPV: negative predictive value.

Characteristics of the hospitals included in the study

Patients were included from the following nine hospitals in Sweden.

Karolinska University Hospital, Solna, Stockholm, and Karolinska University Hospital Huddinge, Stockholm

Karolinska University Hospital is located at two sites, 22 km apart, in Solna and Huddinge. Karolinska University Hospital Solna is situated in the northern part of Stockholm city, and has a yearly attendance at the ED of approximately 74,000. The other site is located south of Stockholm in Huddinge municipality, which is administered by Stockholm County Council. The annual number of visits to the ED in Huddinge is approximately 75,000. During the study period, on-site coronary angiography and percutaneous coronary intervention (PCI) were only available at Huddinge during office hours, but at all times at Solna.

Sahlgrenska University Hospital, Sahlgrenska, Östra and Mölndal, Gothenburg

Sahlgrenska University Hospital was founded in 1997 when three hospitals merged: Sahlgrenska Hospital, Östra Hospital and Mölndal Hospital. All the sites are located in the city of Gothenburg, and the hospital has a total capacity of 2,000 beds. In total, there are approximately 106,000 visits per year to the adult ED.

St. Görans Hospital, Stockholm

St Görans Hospital is centrally located in Stockholm city, and had approximately 77,000 annual visits to the ED during the study period. During this period, on-site coronary angiography and PCI were only available during office hours.

Stockholm South General Hospital, Stockholm

Stockholm South General Hospital is located in the southern part of Stockholm city, and has the largest emergency care unit in the Nordic region. The annual number of visits to the ED is approximately 120,000. At the time of the study, coronary angiography was only available during office hours.

Södertälje Hospital, Stockholm

Södertälje Hospital is located outside Stockholm city, in Södertälje municipality, but this is administered by Stockholm County Council. This hospital has the lowest yearly ED attendance (approximately 32,000) of the hospitals in this study. Södertälje Hospital is the only hospital within Stockholm County that did not provide coronary angiography on-site. Therefore, patients treated at Södertälje Hospital who were in need of a coronary angiography, with or without percutaneous coronary intervention (PCI), were transferred to one of the other hospitals in Stockholm.

Roos A, Holzmann MJ. *Open Heart* 2022; 8:e001682. doi: 10.1136/openhrt-2021-001682