

## **Rapid diagnostic algorithms for NSTEMI**

Maria Rubini Gimenez, MD<sup>1,2</sup>; Nicholas L. Mills, MD, PhD<sup>3</sup>; Christian Mueller, MD<sup>2</sup>;  
on behalf of the Study Group on Biomarkers of the ESC Association for Acute  
Cardiovascular Care.

<sup>1</sup>Department of Cardiology; Heart Center Leipzig, Germany

<sup>2</sup>Department of Cardiology and Cardiovascular Research Institute Basel, University Hospital  
Basel, University of Basel, Switzerland

<sup>3</sup>University/BHF Centre for Cardiovascular Science and Usher Institute, University of  
Edinburgh, Edinburgh, United Kingdom

**Word count: 499**

### **Correspondence to:**

Dr. Maria Rubini Gimenez,  
Department of Internal Medicine/Cardiology  
Heart Center Leipzig at University of Leipzig  
Strümpellstraße 39  
04289 Leipzig  
Germany  
Phone: +49 341 865-1428  
Fax: +49 341 865-1461  
E-mail: [Maria.Rubini@medizin.uni-leipzig.de](mailto:Maria.Rubini@medizin.uni-leipzig.de)

The introduction of high-sensitivity cardiac troponin (hs-cTn) for the first time has allowed the precise quantification of cardiomyocyte injury around the 99<sup>th</sup> percentile and thereby substantially increased the diagnostic accuracy for the detection of non-ST-segment elevation myocardial infarction (NSTEMI) at presentation to the emergency department (ED).<sup>1</sup> Therefore, this simple, inexpensive and highly reproducible tool complements the detailed clinical assessment including chest pain characteristics and the electrocardiogram in all patients with suspected NSTEMI.<sup>2</sup> Higher accuracy at ED presentation has enabled the development and extensive validation of early hs-cTn-based diagnostic algorithms. Some of these include the option for immediate rule-out and/or rule-in only based on the 0h-sample, further reducing the time required for the safe rule-out or rule-in of NSTEMI.<sup>2</sup> The development of these strategies aimed to achieve predefined very high safety (quantified by the negative predictive value [NPV] and sensitivity for NSTEMI) and efficacy (percentage of patients triaged early) for rule-out, as well as improving the positive predictive value (PPV) and specificity for NSTEMI.<sup>1, 2</sup>

Current European Society of Cardiology (ESC) guidelines encourage the use of these triage algorithms as a Class I recommendation for the ESC 0/1h-hs-cTnT/I-algorithm (Figure). The concept of the ESC 0/2h-algorithm is identical to that of the ESC 0/1h-algorithm and is recommended as an alternative strategy.<sup>2, 3</sup> The use of these strategies is very effective and allows an accurate early triage in about 75% of patients: 60% towards rule-out and in 15% towards rule-in of MI.<sup>1</sup> Another well validated rule-out strategy is the High-Sensitivity Troponin in the Evaluation of patients with suspected Acute Coronary Syndrome (High-STEACS) pathway, which uses separate rule-out and sex-specific diagnostic thresholds at presentation with a second measurement within 3hrs if needed.<sup>4</sup> In a randomised trial, implementation of this strategy enabled 71% of patients with suspected acute coronary syndrome to be

discharged from the ED with no increase in hospital reattendance or major adverse cardiovascular events at one year.<sup>4</sup>

Although these strategies simplify the triage of patients in the ED considerably, a proper training of clinicians is of paramount importance to successfully implement these in practice. There are several aspects which need to be highlighted when using one of these rapid diagnostic algorithms for NSTEMI:

- The decision points derived and validated are assay-specific (Figure). Hence, the first step when using these strategies is to elucidate which assay is being used in the institution.<sup>1</sup>
- In many institutions the turn-around time often is longer than 1h. The application of the 0/1h-ESC-algorithm is also possible in these institutions since 1h only refers to the time point of the second blood sample. The nurse team needs to be trained to obtain the 1h-blood draw in all patients independent of the reporting of the 0h-result to maximize efficacy.
- They should be used only in conjunction with full clinical assessment.
- Patients who do not fulfil either rule-out or rule-in criteria remain in the observe zone.<sup>5</sup> An additional hs-cTnT/I measurement at 3h as well as echocardiography are helpful in most of these patients.<sup>2</sup> However, further studies are needed to improve the management of patients in the observe zone.

Other members of the Study Group on Biomarkers of the ESC Association for Acute Cardiovascular Care and contributors to this manuscript include:

Evangelos Giannitsis, MD<sup>1</sup>; Allan S. Jaffe, MD<sup>2</sup>; Kurt Huber, MD<sup>3</sup>; Johannes Mair, MD;<sup>4</sup> Louise Cullen, MD, PhD<sup>5</sup>; Ola Hammarsten, MD, PhD<sup>6</sup>; Martin Möckel, MD<sup>7</sup>; Konstantin Krychtiuk, MD<sup>8</sup>; Kristian Thygesen, MD<sup>9</sup>; Bertil Lindahl, MD;<sup>10</sup>

<sup>1</sup>Department of Cardiology, University Heidelberg, Germany

<sup>2</sup>Mayo Clinic and Medical School, Rochester, Minnesota, USA

<sup>3</sup>Department of Medicine, Cardiology and Intensive Care Medicine, Wilhelminenhospital, and Sigmund Freud University, Medical School, Vienna, Austria

<sup>4</sup>Department of Internal Medicine III – Cardiology and Angiology, Medical University Innsbruck, Austria

<sup>5</sup>Emergency and Trauma Centre, Royal Brisbane and Women`s Hospital, University of Queensland, Australia

<sup>6</sup>Department of Clinical Chemistry and Transfusion Medicine, University of Gothenburg, Gothenburg, Sweden

<sup>7</sup>Division of Emergency Medicine, Charité-Universitätsmedizin Berlin, Germany

<sup>8</sup>Department of Internal Medicine II, Division of Cardiology, Medical University of Vienna, Austria

<sup>9</sup>Department of Cardiology, Aarhus University Hospital, Denmark

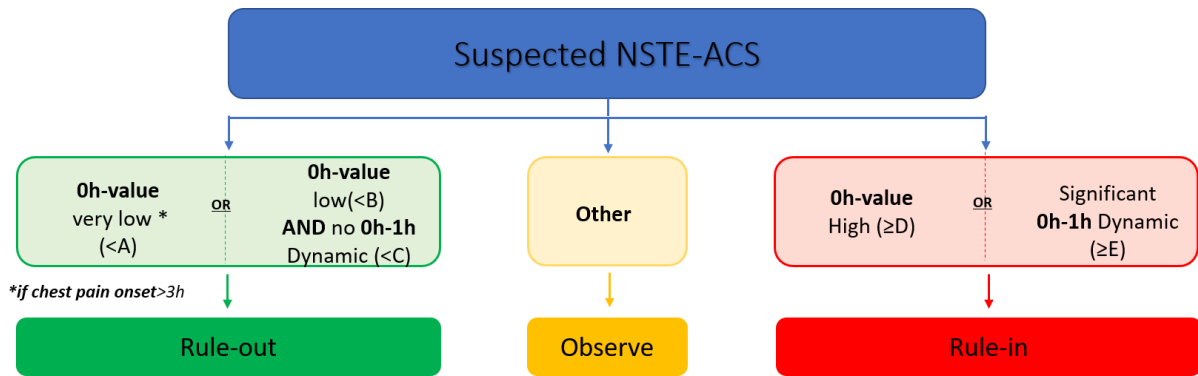
<sup>10</sup>Department of Medical Sciences, Uppsala University, Sweden

## REFERENCES

1. Twerenbold R, Boeddinghaus J, Nestelberger T, Wildi K, Rubini Gimenez M, Badertscher P and Mueller C. Clinical Use of High-Sensitivity Cardiac Troponin in Patients With Suspected Myocardial Infarction. *J Am Coll Cardiol*. 2017;70:996-1012.
2. Collet JP, Thiele H, Barbato E, Barthelémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, Gale CP, Gilard M, Jobs A, Juni P, Lambrinou E, Lewis BS, Mehilli J, Meliga E, Merkely B, Mueller C, Roffi M, Rutten FH, Sibbing D, Siontis GCM and Group ESCSD. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2020.
3. Reichlin T, Schindler C, Drexler B, Twerenbold R, Reiter M, Zellweger C, Moehring B, Ziller R, Hoeller R, Rubini Gimenez M, Haaf P, Potocki M, Wildi K, Balmelli C, Freese M, Stelzig C, Freidank H, Osswald S and Mueller C. One-hour rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. *Arch Intern Med*. 2012;172:1211-8.
4. Anand A, Lee KK, Chapman AR, Ferry AV, Adamson PD, Strachan FE, Berry C, Findlay I, Cruickshank A, Reid A, Collinson PO, Apple FS, McAllister DA, Maguire D, Fox KAA, Newby DE, Tuck C, Harkess R, Keerie C, Weir CJ, Parker RA, Gray A, Shah ASV, Mills NL and Hi SI. High-Sensitivity Cardiac Troponin on Presentation to Rule Out Myocardial Infarction: A Stepped-Wedge Cluster Randomized Controlled Trial. *Circulation*. 2021. 021 Mar 23. doi: 10.1161/CIRCULATIONAHA.120.052380.
5. Nestelberger T, Wildi K, Boeddinghaus J, Twerenbold R, Reichlin T, Gimenez MR, Puelacher C, Jaeger C, Grimm K, Sabti Z, Hillinger P, Kozhuharov N, du Fay de Lavallaz J, Pinck F, Lopez B, Salgado E, Miro O, Bingisser R, Lohrmann J, Osswald S and Mueller C. Characterization of the observe zone of the ESC 2015 high-sensitivity cardiac troponin 0h/1h-algorithm for the early diagnosis of acute myocardial infarction. *Int J Cardiol*. 2016;207:238-45.

### Figure (adapted from Collet et al <sup>2</sup>):

0 h/1 h rule-out and rule-in algorithm using hs-cTn assays in haemodynamically stable patients presenting with NSTEMI to the emergency department. NSTEMI can be ruled out at presentation if the hs-cTn concentration is very low. NSTEMI can also be ruled out by the combination of low baseline levels and the lack of a relevant increase within 1 h. Patients have a high likelihood of NSTEMI if the hs-cTn concentration at presentation is at least moderately elevated or hs-cTn concentrations show a clear rise within the first hour. Cut-offs are assay specific (Table below) and derived to meet predefined criteria for sensitivity and specificity for NSTEMI. NSTEMI = non-ST-segment elevation acute coronary syndrome; hs-cTn = high-sensitivity cardiac troponin;



	A	B	C	D	E
hs-cTnT (Elecys)	5	12	3	52	5
hs-cTnI (Architect)	4	5	2	64	6
hs-cTnI (Centaur)	3	6	3	120	12
hs-cTnI (Access)	4	5	4	50	15
hs-cTnI (Clarity)	1	2	1	30	6
hs-cTnI (Vitros)	1	2	1	40	4
hs-cTnI (Pathfast)	3	4	3	90	20
hs-cTnI (Triage True)	4	5	3	60	8