References

1. Collet, J.P. et al. (2021). Eur Heart J 42(14), 1289 – 367
2. Giannitsis, E. et al. (2021). Clin Res Cardiol, doi: 10.1007/s00392-021-01821-2
3. Ambavane, A. et al. (2017). PLoS One 12(11), e0187662
4. Thygesen, K. et al. (2018). Circulation 138(20), e618 – 51
5. Reichlin, T. et al. (2012) Arch Intern Med 172(16), 1211 – 8
6. Reichlin, T. et al. (2015) CMAJ 187(8), E243 – 52;
7. Mueller, C. et al. (2016) Ann Emerg Med 68(1), 76 – 87
8. Mokhtari, A. et al. (2016) JACC 67(13), 1531 – 40
9. Twerenbold, R. et al.(2019) J Am Coll Cardiol 74(4), 483 – 94
10. Chew, D.P. et al. (2019) Circulation 140(19), 1543 – 56
11. Shiozaki, M. et al. (2017) Int J Cardiol 249, 32 – 5
12. Stoyanov, K.M. et al. (2020). EHJ ACC 9(1), 39 – 51
13. Roffi, M. et al. (2016). Eur Heart J 37(3), 267 – 315
14. Elecsys Troponin T-hs and Troponin T hs STAT method sheets (2021). Product numbers 09315322 190, 09315349 190, 09315357 190

CONCERN-ENERGOMASH

Distributor of Roche Diagnostics
“Concern-Energomash” CJSC
26/8 Azatutyan str., Yerevan, Armenia
Tel.: 011 87 87 17
info@c-e.am | www.c-e.am

Roche

From prolonged time to diagnosis

to accelerated diagnosis of AMI

Faster, evidence-based algorithms for treatment decisions based on the 2020 NSTE-ACS Guidelines from the European Society of Cardiology

WHERE CARE LEADS

Biomarkers for the diagnosis of ACS

Key update from the 2020 NSTE-ACS Guidelines from the ESC

1. Measurement of a **biomarker of cardiomyocyte** injury, preferably **hs-cTn,** is mandatory in all patients with suspected NSTE-ACS[1]

2. If the clinical presentation is compatible with myocardial ischaemia, then a **dynamic elevation** of cTn >99th percentile of healthy individuals indicates Myocardial Infarction (MI)[1]

3. The **ESC 0 /1-h algorithm** is now recommended as the first-choice diagnostic algorithm (Class I B)[1]

4. **As an alternative** to the ESC 0/-1h algorithm, it is recommended to use the ESC **0/2-h algorithm,** if an hs-cTn test with a validated 0/2-h algorithm is available (Class I B)[1]

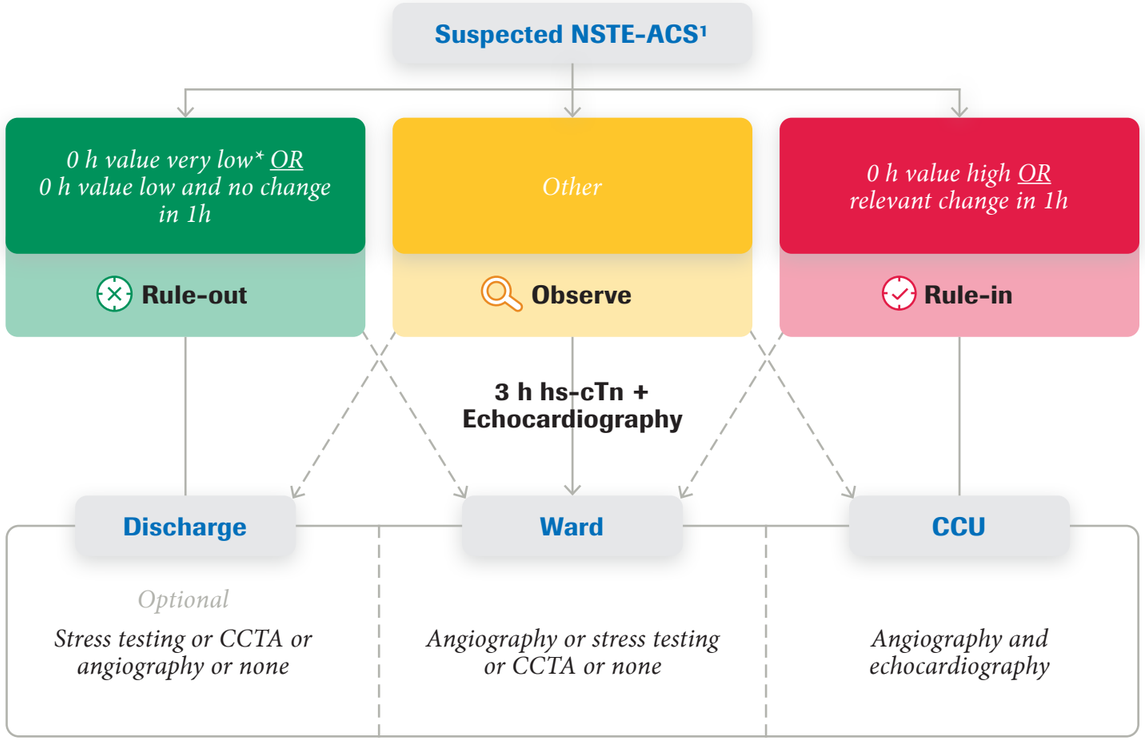
5. The 0/3-h algorithm recommendation was **downgraded** to a Class IIa B recommendation[1]

6. While cTnT-hs and hs-cTnI have comparable diagnostic accuracy, **cTnT-hs** has greater **prognostic** accuracy[1]

7. Biomarkers should always be **used in combination** with **clinical assessment** and **12-lead ECG** in the diagnosis, risk stratification, and treatment of patients with suspected NSTE-ACS[1]

ACS, acute coronary syndrome; ECG, electrocardiogram; ESC, European Society of Cardiology; MI, myocardial infarction; NSTE-ACS, non ST-elevation acute coronary syndrome

The ESC 0 /1-h algorithm to accelerate the time to diagnosis and to drive immediate therapeutic consequences for the diagnosis of ACS



0/1-h algorithm benefits

Reduce length of observation time²

Reduced overall length of ED stay²

Lower hospital & overall AMI diagnostic cost²,³

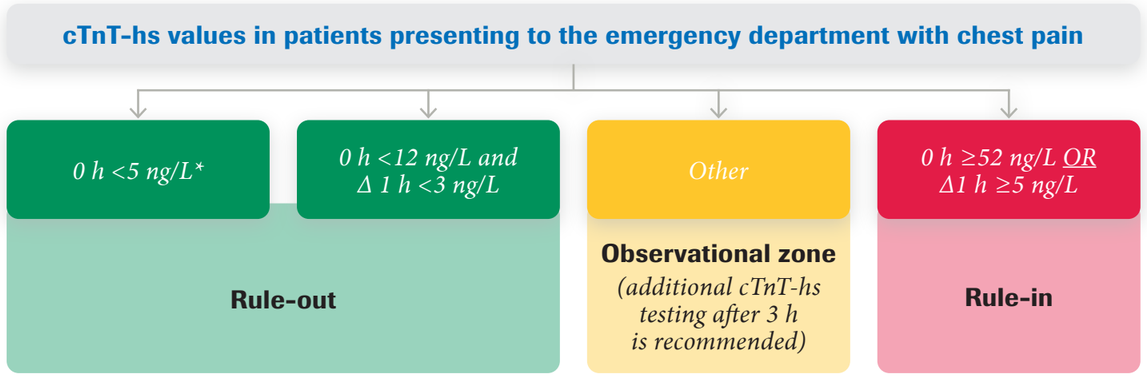
Risk of MI at index visit was <0.3% for the rule-out group, ~10% for the observe group, and >65% for the rule-in group; Risk of 30-day MACE was <0.5% for the rule-out group, 15–20% for the observe group, and >70% for the rule-in group.

* If chest pain onset was >3 h. AMI, acute myocardial infarction; CCTA, coronary computed tomography angiography; CCU, coronary care unit; ECG, electrocardiogram; ED, emergency department; ESC, European Society of Cardiology; MACE, major adverse cardiac event; MI, myocardial infarction; NSTE-ACS, non ST-elevation acute coronary syndrome

The first algorithm to rule-in or rule-out AMI within 0 to 1 h using cTnT-hs is confirmed by the 2020 ESC Guidelines

The ESC 0/1-h algorithm complemented with cut-offs specific for cTnT-hs¹

1 hour

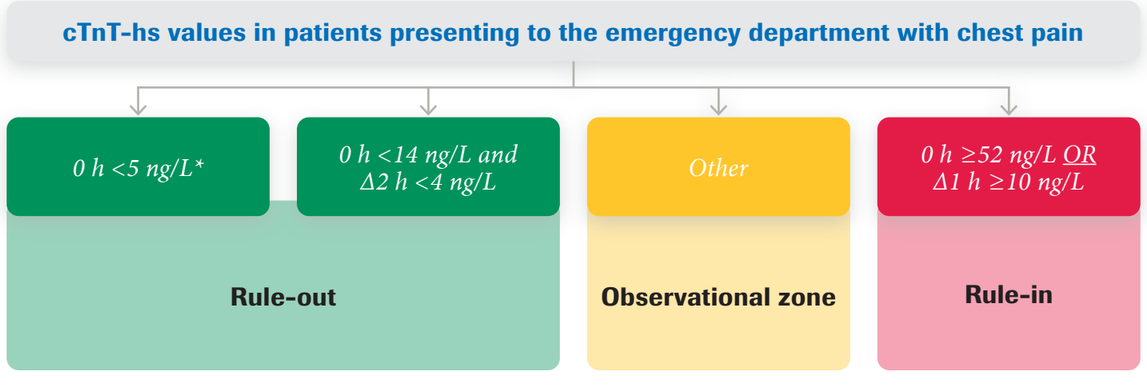


New in the guidelines: The ESC 0/2-h algorithm

Indicated as an alternative to the ESC 0/1-h algorithm

The ESC 0/2-h algorithm complemented with cut-offs specific for cTnT-hs¹

2 hours



* Applicable for chest pain patients with onset longer than 3 h

AMI, acute myocardial infarction; ECG, electrocardiogram ESC, European Society of Cardiology

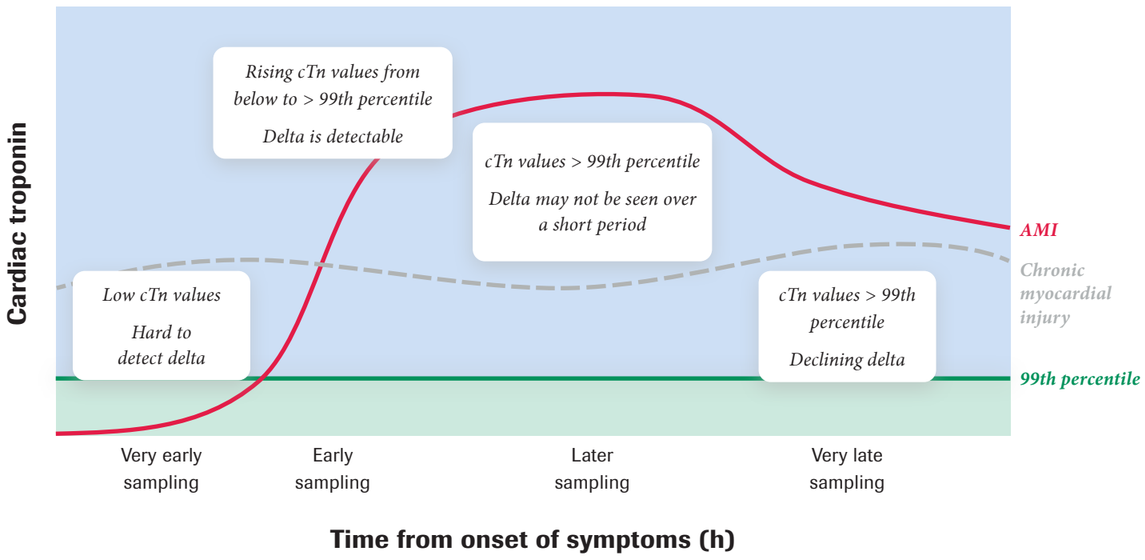
Caveats to consider with rapid algorithms[1]

Algorithms should always be interpreted in conjunction with clinical and ECG findings[1]

Troponin release is time-dependent. An additional cTn measurement at 3 h should be considered in patients presenting <1 h after chest pain onset and triaged towards rule-out[1]

Late increases in cTn concentrations have been described. Serial cTn testing should be carried out if clinical suspicion remains high or in patients with recurrent chest pain[1]

Assessing the rise and/or fall of cTn levels can help differentiate AMI from other conditions associated with cardiomyocyte injury[4]



*Those with very low 0 h concentrations/chest pain onset >3 h

ESC, European Society of Cardiology; MI, myocardial infarction

Practical guidance for the implementation of the ESC 0/1 cTnT-hs algorithm[1]

Collect blood samples for hs-cTn measurements at admission (0 h) and 1 h later[1]

The team should not wait for other clinical details or pending results[1]

The exact time of 0 h blood draw should be recorded to accurately estimate the time window (±10 min) of the 1 h blood draw[1]

In case the 1 h (±10 min) collection is not possible, blood should be collected at 2 h and the 0/2-h algorithm should be used[1]

Take note: Early measurements may seem unnecessary in some patients.* However, evaluating troponin dynamics early accelerates the process of ruling in and ruling out MI.

Timing of the blood draws and time of clinical decision differ

An important point to consider when using the 0/1-h algorithm

The ESC 2020 NSTE-ACS Guidelines recommend the measurement of **cardiac troponins** with **high-sensitivity assays** immediately after admission. The results should be available within 60 minutes of blood sampling (Class I, Level B)[1]

The ESC 0/1-h algorithm is used irrespective of the local turnaround time. In the **0/1-h algorithm,** 0 h and 1 h refer to the **timepoint at which blood is taken.** To calculate the earliest timepoint for clinical decision, the local TAT should be added to the time of blood collection[1]

Compared to other algorithms, the 0/1-h algorithm possesses clinical and economic benefits, independent of the local TAT[1]

Quicker diagnosis + shorter hospital stay = reduced resource utilisation[3]

Fewer blood draws, ECGs and imaging studies are required[3]

ECG, electrocardiogram; ESC, European Society of Cardiology; TAT, turnaround time

The performance and safety of rapid rule-out using the ESC 0/1-h algorithm with cTnT-hs is confirmed by multiple studies[5-11]

Publications and trials using cTnT-hs values for patient assignment to the rule-out zone

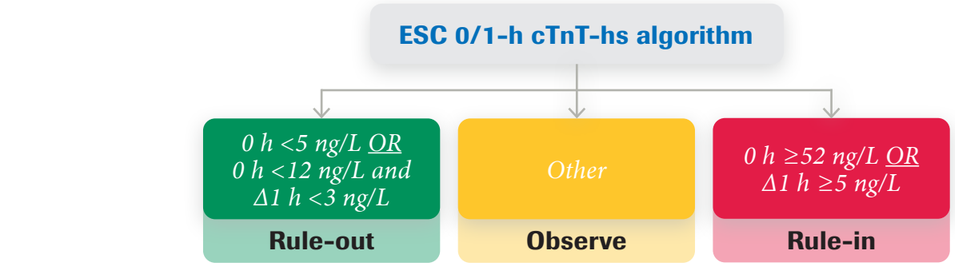
Study	NPV (95% CI)	All-cause mortality or MACE in the rule-out zone
0 h <12 ng/L and Δ 1 h <3 ng/L		
APACE[5]	100%	**30 days all-case mortality: 0.2%** 2 years all-cause mortality: 1.9%
APACE[6]	99,9% (99.3–100%)	**30 days all-case mortality: 0%** 2 years all-cause mortality: 1.1%
TRAPID-AMI[7]	99.1% (98.2–99.7%)	**30 days all-case mortality: 0.1%** 2 years all-cause mortality: 0.7%
Mokhtari et al.[8]	NPV* for 30 days MACE: 99.5% (98.6–99.9%)*	**30 days MACE*: 0.5% and 0% without UA**
0 h <5 ng/L or 0 h < 12 ng/L and Δ 1 h < 3 ng/L		
APACE[9]	100%	**30 days and 1-year all-case mortality: 0.2%**
RAPID-TnT[10]	99.6% (99.0–99.9%) for 30 days death or MI	**30 days all-case mortality and MI: 0.4%**
Shiozaki et al.[11]	100% (96.8–100%)	**30 days all-case mortality: 0%**

cTnT-hs can be used as an aid for early discharge and out-patient management for patients suspected of ACS

The **high NPV** (99.1-100%) of the 0/1-h algorithm and the **low 30-day mortality** (0-0.4%) in the rule-out zone **confirms** the **safety** of this approach for **early discharge**

* When using the extended algorithm adding ECG and patient history as recommended by the ESC guidelines. ACS, acute coronary syndrome; CI, confidence interval; ECG, electrocardiogram; NPV, negative predictive value; MACE, major adverse cardiac event; MI, myocardial infarction; UA, unstable angina

In three prospective studies and more than 8000 patients interventional studies confirm the excellent performance of the 0/1-h algorithm using cTnT-hs[9,10,12]



The ESC 0/1-h cTnT-hs algorithm triages over three-quarters of ED chest pain patients: **75–84% of patients** triaged within 1 hour (plus lab time)

The safety of the ESC 0/1-h algorithm using cTnT-hs is confirmed by the low incidence of 30-day MACE or mortality in rule-out patients*

Twerenbold R et al.[9]

30-day MACE rate:

0.2% in the rule-out group

0.1% among patients triaged to outpatient care†

Chew DP et al.[10]

30-day all-cause death or MI rate:

0.5% in the rule-out group

0.3% among patients discharged directly from the ED

Stoyanov KM et al.[12]

30-day mortality rate:

0.4% in the rule-out group

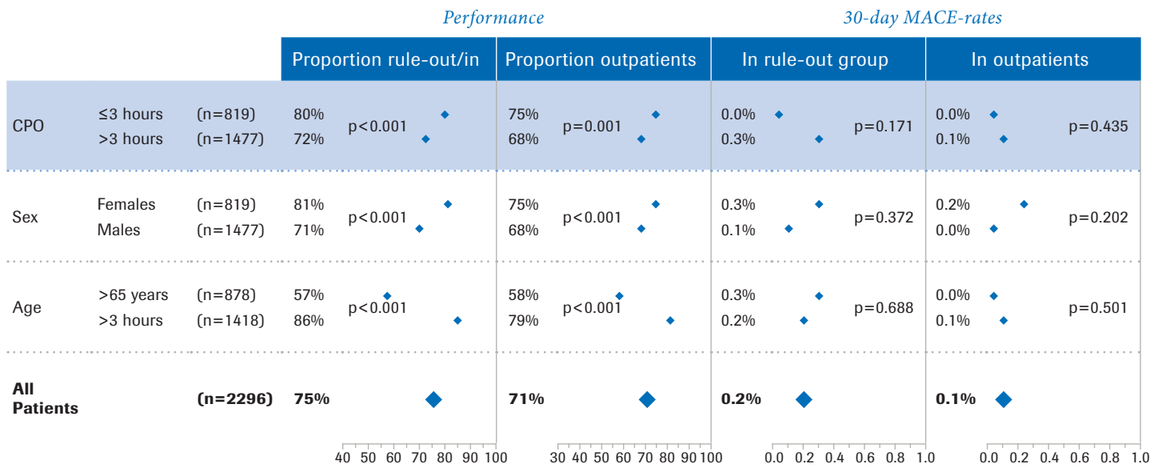
0.08% among patients triaged to outpatient care†

The **low 30-day MACE** rate (0.1-0.3%) among patients discharged directly from the ED confirms the safety of this approach for **early discharge**

* Rule-out group indicates patients recommended to be ruled-out for MI by the algorithm; † Outpatient care indicates patients in which the final management decision made was direct discharge from the ED CI, confidence interval; ED, emergency department; ESC, European Society of Cardiology; MACE, major adverse cardiac events; MI, myocardial infarction

The performance of the ESC 0/1-h algorithm using cTnT-hs is robust in important patient subgroups (e.g. early presenters, sex, age)[9]

Forest plots illustrating efficacy and safety of the ESC 0/1-h cTnT-hs algorithm in pre-defined subgroups[9]



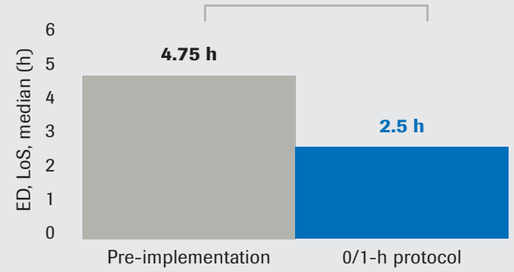
30-day MACE rates were low in all subgroups
For early presenters (CPO ≤3 h), the 0/1-h algorithm triaged **80%** to rule-out or rule-in, with a **0%** 30-day MACE rate in rule-out patients[9]

CPO is the time from onset of chest pain symptoms to patient presentation in the EDCPO, chest pain onset; ED, emergency department; ESC, European Society of Cardiology; MACE, major adverse cardiac events

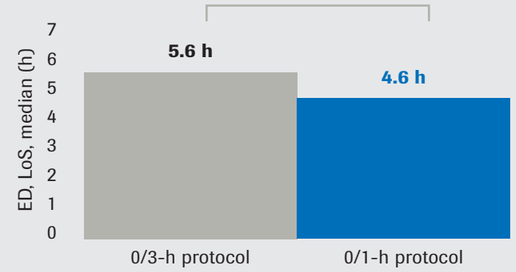
The ESC 0/1-h algorithm using cTnT-hs reduces LoS in ED & acute care[9,10,12]

Median reduction of 1–2 hours of length of stay* compared with standard of care[9,10,12]

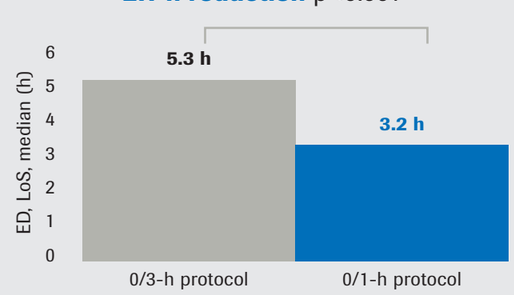
Twerenbold R et al.[9]



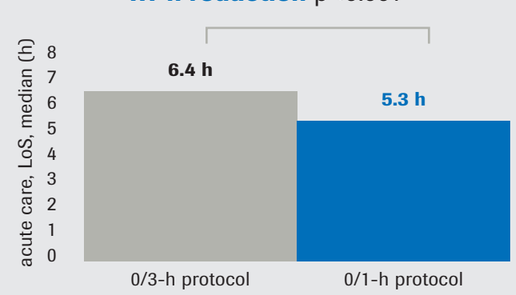
Chew DP et al.[10]



Stoyanov KM et al.[12]



Chew DP et al.[10]



Improves ED patient flow
- Triages **75–84%** of patients to rule-in OR rule-out within 1 hour (plus lab time)[9,10,12]
- Rule-out of AMI possible in **62–72%**[9,10,12] of patients with a NPV of **99.6%**[9]

Shortens length of stay (compared to 0/3-h algorithm) without compromising safety
- Significantly **increases ED discharge** rates compared with the standard of care[9,10,12]
- Reduces ED LoS by 1.0 – 2.25 h[9,10,12]
- Reduces acute care LoS by 1.1 h[12]

*Comparisons are with pre implementation / standard algorithm. AMI, acute myocardial infarction; ED, emergency department; ESC, European Society of Cardiology; LoS, length of stay; NPV, negative predictive value

Conclusions from the three studies[9,10,12]

The implementation of the ESC 0/1-h algorithm using cTnT-hs[13]

cTnT-hs is safe

- Low 30-day event rate 0.2 - 0.5% (MACE, all cause mortality and MI, or mortality)[9,10,12]
- 0.08% 30-day mortality in patients triaged to out-patient care[12]

cTnT-hs is feasible

- 94% algorithm adherence[9]
- 45 minute median reduction in the time between initial and second cTnT-hs sample[12]

cTnT-hs does not increase the use of diagnostic resources[9,10,12]

- Significant reduction in functional cardiac testing[10]
- No increase in coronary angiography[10,12]

Biomarkers as tools for prognostication and risk assessment

Beyond its diagnostic role, it is recommended to measure hs-cTn serially for the estimation of prognosis **(Class I B)**[1]

cTnT-hs and hs-cTnI possess comparable diagnostic accuracy, however, **cTnT-hs has greater prognostic accuracy**[1]

hs-cTn **adds prognostic information** with regards to short- and long-term mortality to clinical and ECG variables[1]

The higher the hs-cTn levels, the greater the risk of death. Serial measurements can be used to **detect peak levels** of cardiac troponin and risk stratify patients with established MI[1]

BNP/NT-proBNP, serum creatinine and eGFR also affect prognosis and should be **measured concomitantly**[1]

ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; NT-proBNP, N-terminal pro-brain natriuretic peptide (BNP)

Conclusions

The 0/1-h algorithm (best option, blood draw at 0h and 1h) and the 0/2-h algorithm (second best option, blood draw at 0h and 2 h) are the preferred rapid algorithms and are recommended with a **Class IB** recommendation[1]

Both algorithms have **data driven assay-specific cut-offs,** derived and validated to achieve predefined performance characteristics, for both rule-out and rule-in of AMI, justifying immediate therapeutic consequences[1]

Multiple hs-cTn assays can be used with both algorithms and are supported by real life studies documenting safe and efficient implementation[1]

The 0/1-h algorithm using cTnT-hs is **validated in numerous prospective trials[9,10,12]**

Roche cTnT-hs is the first hs-cTn assay to introduce a **rapid rule-out claim for early discharge** and **out-patient management** for patients suspected of ACS[14]

ACS, acute coronary syndrome; AMI, acute myocardial infarction

Elecsys® Troponin T hs intended use[14]

Supported by numerous (> 1300) publications and has multiple intended uses

1. Aid in diagnosis
Aid in the differential diagnosis of acute coronary syndrome to identify necrosis, e.g. acute myocardial infarction[14]

5. Selection of therapy and intervention
The test may also be useful for the selection of more intensive therapy and intervention in patients with elevated levels of cardiac troponin T[14]

2. Rapid rule-out
Aid for early discharge and out-patient management for patients suspected of acute coronary syndrome (ACS)[14]

6. Perioperative use
To predict the perioperative risk of major adverse cardiac events and for the aid in diagnosis of (MINS) and PMI in non-cardiac surgeries[14]

3. Risk stratification – ACS
Risk stratification of patients presenting with acute coronary syndrome[14]

7. General population
To aid in stratifying the long-term risk of cardiovascular death, myocardial infarction, coronary revascularization, heart failure, or ischemic stroke and all-cause mortality in asymptomatic individuals[14]

4. Risk stratification – chronic renal failure
Cardiac risk stratification in patients with chronic renal failure[14]

ACS, acute coronary syndrome; AMI, acute myocardial infarction; MI, myocardial infarction; MINS, myocardial injury after non-cardiac surgery; PMI, perioperative myocardial infarction