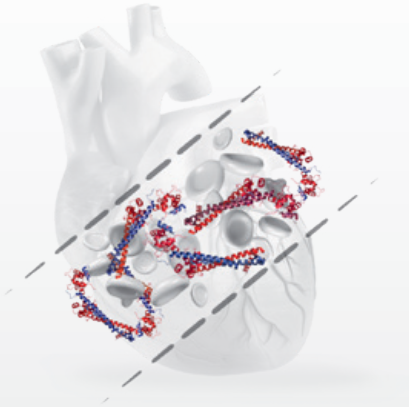
Atellica IM High-Sensitivity Troponin I (TnIH) Assay

A novel prognostic tool expands clinical utility



Introduction

High-sensitivity cardiac troponin (hs-cTn) assays revolutionized management of new-onset chest pain in patients presenting to the Emergency Department (ED). Troponins are quantitative markers of myocardial injury with high specificity due to distinct sequence elements within cardiac troponins I and T that distinguish them from their skeletal troponin isoforms. The improved sensitivity and low-end precision of these high-sensitivity assays support expedient diagnosis for an acute myocardial infarction (AMI) and inform clinical triage in patients presenting with AMI signs/symptoms.

Glossary of terms	
ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
ED	Emergency Department
HF	Heart Failure
SH Atellica IM TnIH	Siemens Healthineers Atellica IM High-Sensitivity Troponin I assay
CVD	Cardiovascular Disease
URL	Upper Reference Limit
hs-cTn	High-Sensitivity Cardiac Troponin

Now, in a first of its kind in the U.S., Siemens Healthineers Atellica IM High-Sensitivity Troponin I (TnIH) assay has been cleared to include a prognostic application in patients presenting to the ED with signs and symptoms of acute coronary syndrome (ACS).

There are potentially valuable implications for management and follow-up in the significant percentage of patients who are not having an event but may have elevated risk of adverse events in the near term (within 30 days to one year). Follow-up at differing time points over one year demonstrated that an initial elevated TnIH result (defined as > overall 99th percentile), is associated with higher rates of unfavorable outcomes compared to those without an elevated TnIH (≤ 99th percentile) in patients presenting with signs and symptoms of ACS who are not diagnosed with AMI.

Monitor risk of all-cause mortality and major adverse cardiac events for up to 365 days

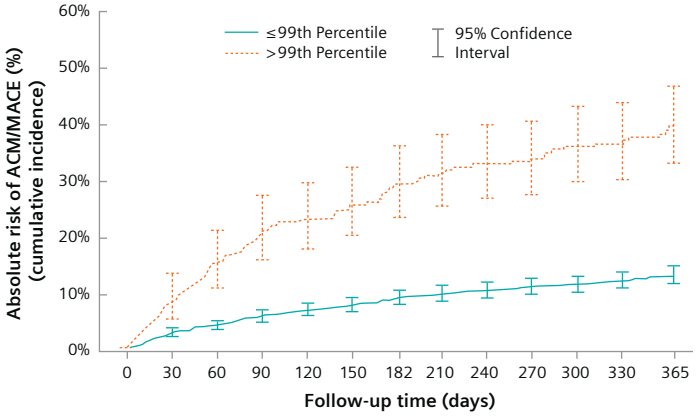


Figure 1. Kaplan-Meier Curves for Population 1 (Lithium Heparin; n = 2064)[11]

SIEMENS Healthineers

Existing claims and use for Atellica IM TnIH

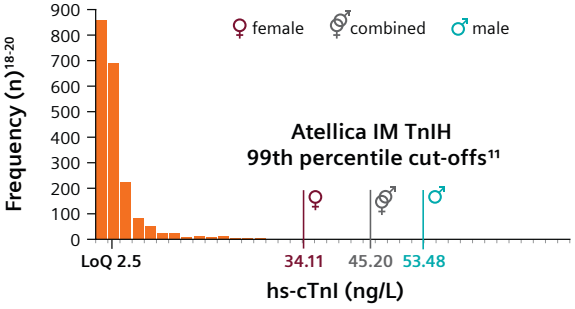
Aiding AMI diagnosis with serial testing in chest pain patients presenting acutely

Supporting an AMI diagnosis

Acute onset chest pain is a frequent reason for patients presenting to the ED.[1-3] Timely diagnosis is vital to identify those experiencing an AMI, and expediently rule out those with a non-AMI etiology.[1-4] Current guidelines recommend serial testing using hs-cTn assays to aid an AMI diagnosis and are preferred due their high specificity and sensitive detection of myocardial damage.[2-5]

The 2018 Fourth Universal Definition of Myocardial Infarction Consensus Document defines a cTn elevation as exceeding the 99th percentile upper reference limit (URL).[4] 99th percentiles are assay-specific and derived from a healthy reference population, for either sex-specific (men/women) values or an overall (combined) value.[3,6,7] Analytically, high sensitivity assays should have detectable results in ≥50% of a healthy reference population (for both men and women) and achieve ≤10% CV at the assay's 99th percentile.[4,6]

Atellica IM TnIH 99th Percentile Cut-Offs[11]



Serial testing to assess for a rise or fall of cTn with at least one value above the 99th percentile is recommended to support diagnosis in chest pain patients with suspected AMI.[2-4] Importantly, cTn results must be considered in the context of other clinical findings to inform decision-making, such as signs of myocardial ischemia.[2-6] Serial comparisons of cTn are an essential component, as a sizable percent of non-AMI patients may have presentation values >99th percentile but lack the significant change pattern associated with AMI.[5,8]

Supporting an AMI exclusion

The improved sensitivity and low-end precision of high sensitivity assays play a crucial role in the ED, **as the majority of chest pain patients are not experiencing an AMI and benefit from an expedient and accurate diagnosis.[2,9]** These patients may be triaged for alternate causes of chest pain or safely discharged following investigation. Serial cTn testing with values ≤99th percentile and/or failing to demonstrate a significant rise or fall are an important component for exclusion of AMI in conjunction with the patient's medical history, clinical presentation, and other findings (such as electrocardiogram).[2,3]

NEW: Prognostic utility for Atellica IM TnIH in patients with signs and symptoms of ACS

While patients diagnosed with AMI are known to be at higher risk of a subsequent event, including another AMI,[9,10] outcomes in patients **who are not diagnosed with AMI** are less clear. Many patients who ultimately are not diagnosed with an AMI have cTn presentation values above the 99th percentile, which may reflect myocardial injury from another etiology.[5,8]

Chronic cTn elevations are associated with poorer outcomes, including increased risk for major adverse cardiac events (MACE) and all-cause mortality (ACM).[4,5] While values >99th percentile can be associated with multiple etiologies (Table 1), in others, no clear risk factor is identified.[4,8]

Cardiac troponin is fundamentally an indicator of myocardial injury independent of cause.[4,12] Outside the U.S., including countries in Europe and Asia, multiple cardiac troponin assays, including SH TnIH on Atellica IM and CI Analyzers, have claims for risk stratification.[13,14] Now, with SH Atellica IM TnIH in the U.S., prognostic assessment can be useful in identifying those at risk of a future adverse cardiac event or death, providing an additional resource for clinical management decisions, such as therapeutic interventions or lifestyle changes.[5,8,15]

Until now, the FDA has not cleared a hs-cTn assay in the U.S. for prognostic use. **SH Atellica IM TnIH is the first assay to receive clearance for a prognostic claim from the FDA,[11] as an indicator of risk in patients with signs and symptoms of ACS.** This offers the potential to inform clinical management and aid in differentiation of higher vs. lower-risk patients for follow-up.

Table 1. Common etiologies linked to elevated cTn.[4,8,11]

Causes of cTn elevation in non-AMI include:
Sepsis, atrial fibrillation, heart failure, pulmonary embolism, myocarditis, myocardial contusion, renal failure, and structural heart disease

>99th Percentile

A simple means to interpret Atellica IM TnIH value for prognostic applications

Cardiovascular disease (CVD) is the leading cause of death in the United States, underscoring the importance of follow-up and optimized clinical management.[10] Chest pain patients who present with signs and symptoms of ACS who are excluded for AMI in the acute setting are often discharged with guidance for outpatient follow-up.[16]

Inclusion of a clear and familiar SH Atellica IM TnIH threshold (>99th percentile) with established prognostic utility offers a novel and additional tool supporting follow-up for these patients. Use of the overall 99th percentile includes both men and women, facilitating easy interpretation. Elevated troponin values can be integrated into the overall clinical findings used to optimize intervention and management decisions to help reduce risk of adverse events.

SH Atellica IM TnIH prognostic claim: study design[11]

Using the SH Atellica IM TnIH assay to assess the ability of an elevated cTn to support identification of patients at higher risk of adverse outcomes, baseline levels of cTn were studied in a population of patients presenting to the ED with signs and symptoms of ACS but who were not diagnosed with AMI. Patients were divided by those with a cTn value >99th percentile versus those ≤99th percentile, using the expected values for the overall 99th percentile as presented in the assay labeling. The study population was further divided by those with a history of incident or prior MACE versus those without.

Outcomes included ACM or MACE, as defined in **Table 2**. **Table 3** defines the specific patient populations used for the investigation and claim. For the populations included in the product insert, the entire population consisted of known/suspected ACS patients without an AMI diagnosis with baseline cTn >99th percentile compared to those with cTn values ≤99th percentile. Analysis included post-test risk for those with a history of incident or prior MACE versus patients lacking a history of incident or prior MACE.

Table 2

All-cause mortality (ACM) includes:	Major Adverse Cardiac Events (MACE) include:	Outcomes assessed at (days):
Death from any cause	Myocardial infarction, urgent revascularization, cardiac death, or heart failure hospitalization	30, 90, 182, 365

Table 3

Population 1 (includes the combined population of 2 and 3)	Population 2	Population 3
Patients **without** an acute MI and with or without a history of MACE	Patients **without** an acute MI and **without** a history of incident or prior MACE	Patients **without** an acute MI **with** a history of incident or prior MACE

SH Atellica IM TnIH and prognostic performance: outcomes over time[11]

Figure 2 shows the follow-up assessment intervals used in all three analyzed patient populations.

Figure 2. Risk of Major Adverse Cardiac Events (MACE) or all-cause mortality (ACM)

Observations included:

At one month (30 days)

- In patients **with** a history of incident or prior MACE, a higher risk of events (9.5%) was observed for those with an elevated troponin compared to those without (6.1%) (Figure 3a).
- Patients **without** a history of incident or prior MACE had only a 0.5% risk of experiencing an event within 30 days when initial presentation of cTn was ≤99th percentile compared to a 5.7% risk (~10-fold higher incidence) if baseline TnIH was elevated (Figure 3b).

Figure 3a. Population 3: Entire population excluding subjects with adjudicated AMI and including those with history of incident or prior MACE (Lithium Heparin; n = 874)[11]

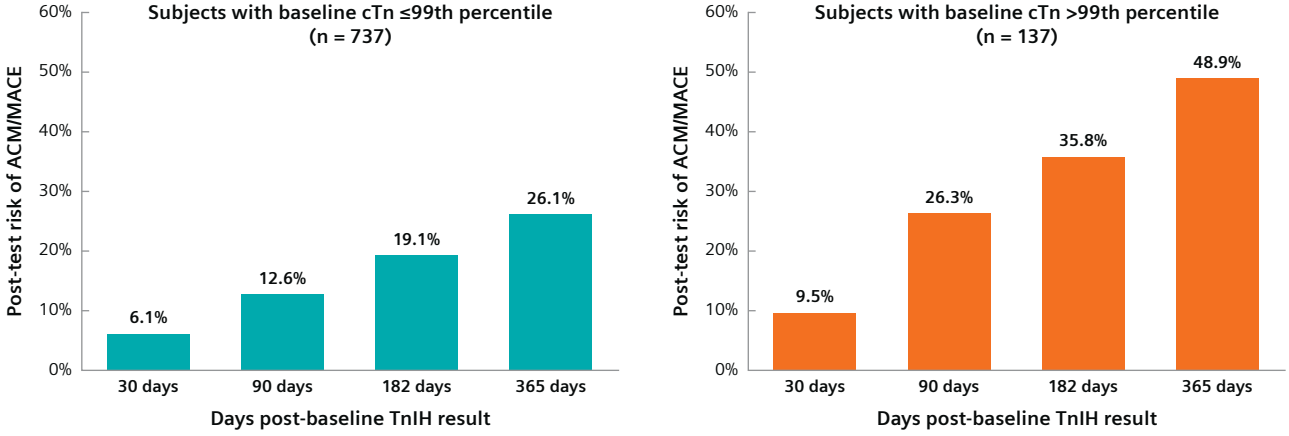
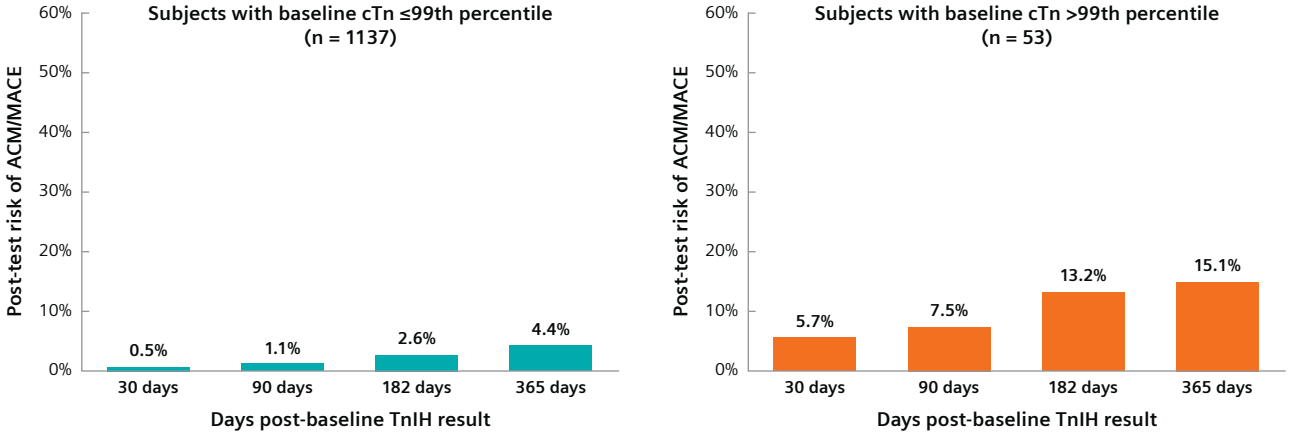


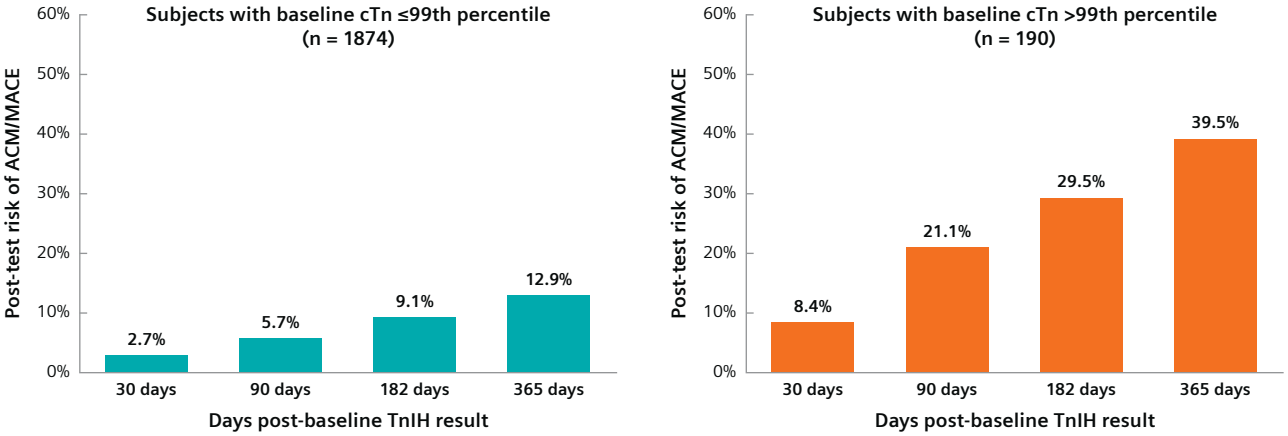
Figure 3b. Population 2: Entire population excluding subjects with adjudicated AMI as well as history of incident or prior MACE (Lithium Heparin; n = 1190)[11]



Events increased over time

Increased risk of events over time was observed in the overall population excluding subjects with adjudicated AMI when comparing patients with elevated troponin to those with a baseline ≤99th percentile.

Figure 4. Population 1: Entire population excluding subjects with adjudicated AMI (Lithium Heparin; n = 2064)[11]



At one year (365 days)

- Patients **with** a history of incident or prior MACE and an elevated baseline cTn had a risk of 48.9% of ACM/MACE within one year, while those without elevated troponin had a risk of 26.1% (Figure 3a).
- In patients **without** a history of incident or prior MACE, ~3-fold higher risk of events was observed in the population with an elevated baseline cTn compared to the population without an elevated baseline troponin (15.1% vs. 4.4%) (Figure 3b).

Prognostic implications: Following patients along the care continuum from the acute into the outpatient setting

The incorporation of cTn as a prognostic indicator in the overall assessment and management of patients with signs and symptoms of ACS may find application in both the ED and the outpatient setting.

Acute/ED: The differences in post-test risk observed at 30 days associated with elevated cTn values could aid risk assessment and inform healthcare management decisions in the acute setting. Implications may include risk of readmission for the same chief complaint within 30 days which may have a financial impact on reimbursment.[17]

Outpatient: Elevated cTn in an at-risk patient (from the ED) could be integrated into other clinical findings and assessments utilized for ongoing healthcare management decisions that could include therapy, lifestyle, and related risk-reduction interventions.

Conclusion

Using the SH Atellica IM TnIH assay, integration of cTn values as a prognostic indicator in patients presenting with signs and symptoms of ACS provides a new tool for patient management with implications in both the acute and subsequent outpatient settings. The ability to identify patients at a higher versus lower risk may inform clinical judgment and holds particular promise for application in the ongoing management of patients as they undergo follow-up. Mitigation or prevention of cardiovascular events or all-cause mortality with effective intervention strategies is a core component of improved outcomes.

For more information, please contact your Siemens Healthineers representative for details on the Atellica cardiac portfolio.

References

1. Hsia, R.Y. et al. A National Study of the Prevalence of Life-Threatening Diagnoses in Patients with Chest Pain. JAMA Internal Medicine July 2016 Volume 176, Number 7; 1029-1032.
2. Gulati, M., Levy, P. D., Mukherjee, D., Amsterdam, E. A., Bhatt, D. L., & Birtcher, K. K. (2021). 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: A report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. Circulation, 144, e368–e454.
3. Sandoval, Y. et al. High-Sensitivity Cardiac Troponin and the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guidelines for the Evaluation and Diagnosis of Acute Chest Pain. Circulation. Volume 146, Issue 7, 16 August 2022; Pages 569-581
4. Thygesen K. et al. Fourth universal definition of myocardial infarction (2018). J Am Coll Cardiol 2018;72:2231–64.
5. Raber, I. et al. Test in Context: Interpretation of High-Sensitivity Cardiac Troponin Assays in Different Clinical Settings. JACC. 2021 Mar, 77 (10); 1357–1367.
6. Apple, F.S. et al. Sex-Specific 99th Percentile Upper Reference Limits for High Sensitivity Cardiac Troponin Assays Derived Using a Universal Sample Bank. Clinical Chemistry, Volume 66, Issue 3, March 2020, Pages 434–444.
7. Aakre, K.M. Mair, J., Ravkilde, J., IFCC Committee on Clinical Application of Cardiac Bio-Markers. Analytical Considerations in Deriving 99th Percentile Upper Reference Limits for High-Sensitivity Cardiac Troponin Assays: Educational Recommendations from the IFCC Committee on Clinical Application of Cardiac Bio-Markers. Clinical Chemistry 68:8; 1022–1030.
8. Eggers, K.M. et al. Cardiac Troponin Elevation in Patients Without a Specific Diagnosis. JACC, Vol. 7 3, No. 1, 2019; Jan. 8/15: 1–9.
9. Holzmann, M.J. et al. Recurrent myocardial infarction and emergency department visits: a retrospective study on the Stockholm Area Chest Pain Cohort. Open Heart 2023;10:e002206.
10. Nair, R. et al. Characteristics and Outcomes of Early Recurrent Myocardial Infarction After Acute Myocardial Infarction. J Am Heart Assoc. 2021;10:e019270.
11. Siemens Healthineers. Atellica IM High-Sensitivity Troponin (TnIH) IFU 11200498, Rev. 10. 2024-09.
12. Kaier, T.E. et al. Cardiac troponin and defining myocardial infarction. Cardiovascular Research (2021) 117, 2203–2215.
13. Roche. Elecsys Troponin I STAT instructions for use for cobas e 411,601,602. 2021-02, V 9.0. Available from: https://elabdoc-prod.roche.com/eLD/web/global/en/home. [accessed 2024 Oct. 1]
14. Abbott. Stratifying Future Cardiac Risk ADD-122047-GBL-EN. Available from: https://www.corelaboratory.abbott/int/en/offerings/segments/cardiac/risk-stratification. [accessed 2024 Dec. 9]
15. Park, J.E. et al. Cardiac troponin I and the risk of cardiovascular or non cardiovascular death in patients visiting the emergency department. Sci Rep 11, 17461 (2021).
16. Writing Committee; Kontos MC, de Lemos JA, Deitelzweig SB, Diercks DB, Gore MO, Hess EP, McCarthy CP, McCord JK, Musey PI Jr, Villines TC, Wright LJ. 2022 ACC Expert Consensus Decision Pathway on the Evaluation and Disposition of Acute Chest Pain in the Emergency Department: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2022 Nov 15;80(20):1925-1960.
17. Centers for Medicare & Medicaid Services. Hospital Readmissions Reduction Program. Available from: https://www.cms.gov/medicare/quality/value-based-programs/hospital-readmissions. [accessed 2024 Dec. 9]
18. Data on file.
19. Lithium Heparin plasma samples.
20. Healthy patient population.

This clinical brief is intended for U.S. audiences only.

Siemens Healthineers Headquarters
Siemens Healthineers AG
Siemensstr. 3
91301 Forchheim, Germany
Phone: +49 9191 18-0
siemens-healthineers.com

Published by
Siemens Healthcare Diagnostics Inc.
Core Lab Solutions
511 Benedict Avenue
Tarrytown, NY 10591-5005
USA
Phone: +1 914-631-8000

Published by Siemens Healthcare Diagnostics Inc. · CLS-25-4045-76 · QR700022004 · 04-2025 · ©Siemens Healthcare Diagnostics Inc., 2025