PATHFAST™

hs-cTnI
high sensitivity troponin I

IFCC & ESC compliant

0/1 h NSTEMI rule-out/rule-in algorithm

Results in < 17 minutes

POCT - whole blood/plasma

<17 min

PATHFAST

MITSUBISHI CHEMICAL EUROPE

LSI Medience Corporation

a subsidiary of MITSUBISHI Chemical Holdings

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PATHFAST™ hs-cTnI is a chemiluminescent enzyme immunoassay (CLEIA) for quantitative measurement of cardiac troponin I (cTnI) concentration in whole blood or plasma at the point of care (POC).

Low concentrations of cTnI can be analysed by using high sensitivity cardiac troponin (hs-cTnI) assays which meet the criteria defined by IFCC and ESC (1,2). PATHFAST™ provides high accuracy and precision of test results similar to central lab analyser, combined with the flexibility of a POCT assay within 17 minutes out of whole blood and plasma by all in one cartridge solution.

The new PATHFAST™ hs-cTnI assay fits for the recommendations on the IFCC and ESC guidelines (2015) for the use of high sensitivity troponin assays (1,2).

Clinical benefits of hs-cTn assays

hs-cTnI assays detect troponin levels at low concentrations with high accuracy and precision at the earliest point of time. They measure low levels of troponin released by ischemia/micro-necrosis (Fig. 1) and allow even detection and quantification of troponin levels of healthy individuals (4).

The European Society of Cardiology (ESC) recommend the use of hs-cTnI assays (2,3) for early rule-in and rule-out of Acute Myocardial Infarction (AMI) and differentiation from patients with non-coronary artery cardiac diseases.

In addition to the diagnosis of AMI, detection of low cardiac troponin levels may make it possible to predict information (risk stratification) in terms of short- and long term mortality of patients (5).

In clinical studies PATHFAST™ hs-cTnI has been evaluated for a 99th percentile upper reference limit of 29.0 ng/L at an imprecision of 6.1%, which is less than 10% and fits for the criteria of hs-cTnI, declared by IFCC (1).
For PATHFAST™ hs-cTnI assay the 99th percentiles values were determined in 734 healthy individuals and are listed in Table 1. Gender specific 99th percentile cut offs for overall, females and males are 27.9 ng/L (this value is not significantly different from the FDA cleared overall 99th percentile of 29.0 ng/L before exclusion of individuals with abnormal NT-proBNP, HbA1c and eGFR), 20.3 ng/L, and 29.7 ng/L respectively (6).

Troponin concentrations were measured with the PATHFAST™ hs-cTnI assay in EDTA plasma.

Samples from 993 patients obtained at 0 hour, 1 hour and 3 hours after admission to the Chest Pain Unit (CPU) with suspicion of acute coronary syndrome, were used. 219 AMI patients were identified (23.5%) by two independent cardiologists with blinded cTnI values.

The ROC analysis for the discrimination between AMI and non-AMI patients including the clinical sensitivity and specificity, as well as the Positive and Negative Predictive Values (PPV and NPV) based on the 99th percentile value are explained in Table 2 for PATHFAST™ hs-cTnI assay. Comparison with one established central laboratory methods (troponin I) showed comparable diagnostic validity for AMI (NSTEMI and STEMI) (Fig. 2A) and NSTEMI patients (Fig. 2B) (7).

PATHFAST™ hs-cTnI assay offers the opportunity for chest pain units and emergency units to test hs-cTnI in less than 17 minutes.

**Criteria for a high sensitivity cTn assays**

**Recommendation from IFCC (1)**

- 99th percentile of hs-assays should be measured with an analytical imprecision of <10% CV
- hs-cTn assays should measure cTn above the limit of detection (LOD) in 50% of healthy individuals
- Gender specific 99th percentile values should be established for men and women

**Recommendation from ESC guideline (2,3)**

New ESC guidelines of 2015 advises to use 0 h /3 h rule-out or a 0 h /1 h rule-in/rule-out algorithm by using high sensitivity troponin assays as an alternative to the established 0 h /3 h /6 h procedere (2).

**Table 1: Gender specific 99th percentile by PATHFAST™ hs-cTnI assay**

<table>
<thead>
<tr>
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<th>N</th>
<th>Gender specific 99th percentile (ng/L)</th>
<th>% measurable concentrations &gt; LoD</th>
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<tr>
<td>Overall</td>
<td>734</td>
<td>27.9</td>
<td>n= 487 (66.3%)</td>
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<tr>
<td>Males</td>
<td>382</td>
<td>29.7</td>
<td>n= 301 (78.8%)</td>
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<tr>
<td>Females</td>
<td>352</td>
<td>20.3</td>
<td>n= 186 (52.8%)</td>
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Gender specific 99th percentile and measurable number of healthy subjects between LoD and 99th percentile after exclusion of individuals with abnormal NT-proBNP, HbA1c and eGFR (6)

**Fig 2A:** Comparison ROC of Method A for AMI (STEMI and NSTEMI) patients

**Fig 2B:** Comparison ROC of Method A for NSTEMI patients

**Tab. 2: ROC analysis for diagnosis of AMI at 0,1,3 hour after admission**

<table>
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<tr>
<th>Time point after admission</th>
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<th>1h</th>
<th>3h</th>
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<tr>
<td>RO-AUC</td>
<td>0.901</td>
<td>0.949</td>
<td>0.964</td>
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<tr>
<td>Sensitivity, % (95% CI)</td>
<td>65 (58-72)</td>
<td>81 (75-86)</td>
<td>91 (86-94)</td>
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<td>Specificity, % (95% CI)</td>
<td>92 (90-94)</td>
<td>93 (90-94)</td>
<td>91 (89-93)</td>
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<tr>
<td>PPV, % (95% CI)</td>
<td>73 (66-79)</td>
<td>77 (71-82)</td>
<td>75 (69-80)</td>
</tr>
<tr>
<td>NPV, % (95% CI)</td>
<td>89 (86-91)</td>
<td>94 (92-96)</td>
<td>97 (96-98)</td>
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</table>

Diagnostic performance criteria of PATHFAST™ hs-cTnI (7)
Diagnostic algorithms for PATHFAST™ hs-cTnI

The ESC guidelines recommended rule-in and rule-out algorithms using hs-cTn assays in patients admitted with suspected NSTEMI to the ED (2).

Fig. 3: Schematic depiction of rule-in and rule-out algorithms

0 h / 1 h Rule-in algorithm of NSTEMI for PATHFAST™ hs-cTnI

According to the ESC guideline rule-in is possible already at admission (0h) if the value is below a cutoff level (A) and if onset of chest pain > 3h. Regarding the LoD of 2.3 ng/L preliminary study data using a cutoff level A of chest pain > 3 h. Regarding the LoD of 2.3 ng/L preliminary results regarding the LoD of 2.3 ng/L preliminary results using only baseline (0 h) hs-cTnI levels have been examined for 669 patients with suspected NSTEMI and NPVs between 98.9% and 100%. Rule-out is possible by the combination of a baseline level A obtained from patients with onset of chest pain > 3 h.

Rule-out is possible by the combination of a baseline level B and below of an increase within 1 hour (0h to 1 h) ≥ D (Table 4) or the hs-cTn concentration shows a rise within the first hour above the delta cut off level ≥ E (Table 5). The PPVs for rule-in NSTEMI obtained from validation cohorts meeting the rule-in criteria were 75-80% (2). PATHFAST™ hs-cTnI fulfilled these conditions in a clinical study with 669 patients with suspected NSTEMI. Cut off values with PPVs between 75.2% and 78.6% have been identified (7). Regarding the clinical situation of the individual patient the user may decide which cut off values may be applicable for optimal rule-out or rule-in.

This preliminary cutoff level of < 3 ng/L may be used only with caution for rule-out at admission because patients with onset of chest pain > 3 h were not identified in the study. Rule-out at admission may be performed using a final cutoff level A obtained from patients with onset of chest pain > 3 h.

0 h / 1 h Rule-out algorithm of NSTEMI for PATHFAST™ hs-cTnI

A rule-out of NSTEMI is possible if the hs-cTn value at admission (0h) is measured above of a cut off level ≥ D (Table 4) or the hs-cTn concentration shows a rise within the first hour above the delta cut off level ≥ E (Table 5). In large validation cohorts the NPVs for rule-out of NSTEMI exceeded 98% (2). For PATHFAST™ hs-cTnI the following cut off levels have been examined with NPVs between 98.9% and 100% (7).
**Instrument type**
Desktop Immunoassay Analyzer

**Throughput**
Up to 6 samples or parameters per run

**Measuring time**
<17 minutes for 6 samples using emergency markers or PATHFAST™ Presepsin

**Sampling material**
Whole blood, plasma, serum

**Measuring principle**
Chemiluminescence enzyme immunoassay technology (CLEIA) and Magtration™ technology.

**Reaction temperature**
37 °C

**Sample volume**
100 µl

**Data storage**
Patient data: 1000, QC data: 1800, CAL data: 300

**Data transfer**
ASTM and Fixed standard

**Weight**
28 kg

**EL requirements**
100 – 240 V AC (50/60 Hz)

**Power consumption**
360 VA

**Monitor/keyboard**
LCD touch-screen

**Printer**
Integrated

**PC**
Integrated, Handheld Barcodereader included

**Interface**
RS-232C and Ethernet Port

**Calibration**
Factory calibration, 2-point calibration every 4 weeks

**24-h operation (stand-by)**
Recommended

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**References**

   IFCC educational materials on selected analytical and clinical applications of high sensitivity cardiac troponin assays. Clin Biochem 2015; 48: 201-203


   Third Universal Definition of Myocardial Infarction. Eur Heart J 2012; 33: 2551-256

   Cardiac biomarkers of acute coronary syndrome: from history to high-sensitivity cardiac troponin. Intern Emerg Med 2017;12: 147-155

   Troponin I and cardiovascular risk prediction in the general population: the BiomarCaRE consortium. Eur Heart J 2016; 37: 2428-2437

   Validation of high-sensitivity performance for a United States Food and Drug Administration cleared cardiac troponin I assay. Clin Biochem. 2018 Jun; 56:4-10

   Diagnostic evaluation of a new high-sensitivity point-of-care troponin I assay. (Personal Communication from the University Heart Center Hamburg, Germany)
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<thead>
<tr>
<th>Product List</th>
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