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Roche CARDIAC POC Troponin T **cobas®**

REF 07007302 190

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SYSTEM cobas h 232

English

Intended use

Quantitative immunological test for the detection of cardiac troponin T in heparinized venous blood for use with the **cobas h 232** instrument. The test is intended as an early aid in diagnosis of acute myocardial infarction and identification of patients with an elevated mortality risk.

Summary

Troponin T (TnT) is a component of the contractile apparatus of the striated musculature. Although the function of TnT is the same in all striated muscles, TnT originating exclusively from the myocardium (cardiac TnT, molecular weight 39.7 kD) clearly differs from skeletal muscle TnT. As a result of its high tissue specificity, cardiac TnT (cTnT) is a cardio-specific, highly sensitive marker for myocardial damage.¹ cTnT increases approximately 3-4 hours after acute myocardial infarction (AMI) and may persist up to 2 weeks thereafter.^{2,3} In contrast to ST-elevation myocardial infarction (STEMI), the diagnosis of non-ST elevation myocardial infarction (NSTEMI) heavily relies on the cardiac troponin result. The medical value of cTnT in the early diagnosis of AMI has been demonstrated in numerous studies, notably the APACE⁴ and TRAPID-AMI⁵ trials and captured in guidelines^{6,7}. Elevated levels of cTnT correlate with the severity of coronary artery disease and to poor outcome independent of natriuretic peptide (BNP or NT-proBNP) levels.^{8,9,10,11} Myocardial cell injury leading to elevated cTnT concentrations in the blood can also occur in other clinical conditions such as myocarditis¹², heart contusion¹³, pulmonary embolism¹⁴ and drug-induced cardiotoxicity¹⁵.

Roche CARDIAC POC Troponin T allows for early detection of cTnT in the pre-hospital setting such as general practitioner's office, ambulances as well as in the Emergency Department.

In a study by Stengaard et al.¹⁶, the cTnT level was determined by paramedics in the ambulance in patients with ongoing or prolonged periods of chest discomfort within the past 12 hours, acute dyspnea in the absence of known pulmonary disease, or a clinical suspicion of AMI. In total, 985 patients were included of which 200 were later diagnosed to have AMI. A cTnT concentration > 50 ng/L was found in 113 subjects of whom 72 (68 %) had AMI. A pre-hospital TnT value > 50 ng/L was highly predictive of mortality (follow-up of 16.5 and 20.7 months), irrespective of whether an AMI was diagnosed.

In situations as described in this study¹⁶, the pre-hospital cTnT value can be used as an early aid in the diagnosis of AMI and thus in the decision to which hospital to take the patient for appropriate treatment. Diagnosis of AMI is made together with evidence of myocardial ischemia (symptoms, ECG changes or imaging results) according to clinical guidelines.⁶ The data also suggest that the cTnT value can be used in the Emergency Department setting as an early aid in the diagnosis of AMI, allowing patients to be directed to the appropriate department. A cTnT result of less than 50 ng/L does not rule out myocardial infarction because the release of cTnT from the damaged myocardial cells into the circulating blood occurs with time delays that vary from person to person and also because of lower cutoffs recommended for rule-out.⁵ Both typical and atypical symptoms in connection with a cTnT result of less than 50 ng/L call for the application of further diagnostic measures, including repeated cTnT tests.

Test principle

The Roche CARDIAC POC Troponin T test contains two monoclonal antibodies specific to cardiac troponin T (cTnT): one gold-labelled, the other biotinylated. The antibodies form a sandwich complex with the cTnT in the blood. Following removal of erythrocytes from the sample, plasma passes through the detection zone in which the gold-labelled cTnT sandwich complexes accumulate and the positive signal is displayed as a reddish line (the signal line). Excess gold-labelled antibodies accumulate along the control line, signalling that the test was valid. The intensity of the signal line increases in proportion to the troponin T concentration.

The optical system of the instrument detects the two lines and measures the intensity of the signal line. The integrated software converts the signal intensity to a quantitative result and shows it in the display.

Reagents

One test contains:

Biotinylated mouse monoclonal anti-troponin T antibodies 0.23 µg
Gold-labelled mouse monoclonal anti-troponin T antibodies 0.11 µg
Buffer and non-reactive components 2.3 mg

Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

Operating conditions

Perform the measurement between 18-32 °C and 10-80 % relative humidity.

Storage and stability

Until the printed expiration date at 2-8 °C.

Up to 1 week at room temperature (15-25 °C).

The test can be used immediately after removal from the refrigerator.

The test must be used within 15 minutes once the pouch has been opened.

Sample stability: 8 hours at room temperature. Do not refrigerate or freeze sample.

Specimen collection and preparation

Use **heparinised venous whole blood** only.

Do not use other anticoagulants, capillary blood, serum or plasma, blood collection tubes containing EDTA, citrate, sodium fluoride or other additives.

The following heparin blood collection tubes have been tested in the performance evaluation: Sarstedt Monovette. Note: only tubes without separating gel are suitable.

No data is available for blood collection tubes supplied by other manufacturers. An influence on the test result in individual cases cannot be ruled out.

Sample volume: 150 µL

Materials provided

- REF 07007302190, Roche CARDIAC POC Troponin T
- 1 code chip

Materials required (but not provided)

- REF 11622889190, Roche CARDIAC Pipettes, 20 disposable syringes (150 µL)
- REF 07089643190, Roche CARDIAC POC Troponin T Control (2 x 1 mL)
- REF 04880668190, Roche CARDIAC IQC
- REF 04901126190, **cobas h 232** instrument, software version ≥ 03.00.02, serial number ≥ KQ0120000
- REF 04901142190, **cobas h 232** instrument with scanner, software version ≥ 03.00.02, serial number ≥ KS0210000
- General laboratory equipment

Calibration

The Roche CARDIAC POC Troponin T test is standardized against the Elecsys Troponin T hs test.

The instrument automatically reads in the lot-specific calibration data from the code chip, eliminating the need for calibration by the user.

Lot code

Every kit contains a lot-specific code chip. The instrument display prompts the user to insert the chip. To ensure that the code chip and test strip lot match, compare the lot number in the display with the number on the code chip. The code chip provides the instrument with all required lot-specific information. An error message is displayed if the wrong code chip is inserted for a test strip lot.

Quality control

For quality control, use Roche CARDIAC POC Troponin T Control.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.



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Calculation

The instrument automatically calculates the concentration of each sample. The reaction time for the Roche CARDIAC POC Troponin T test to display a quantitative result is 12 minutes. In addition, approximately 2 minutes are required for sample detection.

Limitations - interference

The assay is unaffected by icterus (bilirubin ≤ 20 mg/dL), hemolysis (Hb ≤ 200 mg/dL), lipemia (triglycerides ≤ 1000 mg/dL), haematocrit values in the range of 35-50 %, and biotin ≤ 30 ng/mL.

Criterion: Recovery within ± 15 % of initial value at troponin T concentrations ≥ 40 -2000 ng/L.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 110 IU/mL.

High concentrations of lipoic acid (e. g. in pharmaceuticals or as food additive) can lead to lower measurement values.

The cross-reactivity with h-skeletal muscle Troponin T is < 0.1 % for cross-reactant concentrations tested up to 1000000 ng/L.

There is no high-dose hook effect at analyte concentrations up to 500000 ng/L.

At very high concentrations of troponin T the control line may fail to appear, and the instrument may display an error message. In this case, the test must be carried out using another method, like the Elecsys Troponin T hs test.

Patient samples may contain heterophilic antibodies which could react in immunoassays to give falsely elevated or decreased results. Reasons for the presence of heterophilic antibodies might be for example elevated levels of rheumatoid factors or the treatment of patients with monoclonal mouse antibodies for therapeutic or diagnostic purposes.

The Roche CARDIAC POC Troponin T test contains ingredients that minimise interference from heterophilic antibodies. However, complete elimination of interference from all samples cannot be guaranteed.

Interferences caused by pharmaceuticals at therapeutic concentrations are not known.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Measuring range

40-2000 ng/L

Values below 40 will be displayed as Trop T < 40 ng/L

Values above 2000 will be displayed as Trop T > 2000 ng/L

Expected values

The pre-hospital study¹⁶ described in the Summary section showed the following outcome:

- 68 % of the patients with a troponin T value > 50 ng/L had an AMI.
- A troponin T value > 50 ng/L was highly predictive of mortality.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the instruments are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability was measured with 3 lots of Roche CARDIAC POC Troponin T tests and heparinised human blood. The upper one-sided 95 % confidence limit of the variation coefficients was below 20 % over the entire measurement range. Intermediate precision was measured with the Roche CARDIAC POC Troponin T Control in 5 different hospitals. The upper one-sided 95 % confidence limit of the variation coefficients was below 20 %.

Method comparison

A comparison of 3 lots of the Roche CARDIAC POC Troponin T test with the Elecsys Troponin T hs test in a clinical patient population showed slopes between 0.80 and 1.20.

References

- 1 European patent 394816 and US patent 6376206 by Roche Diagnostics GmbH. Specific antibodies to Troponin T, their production and use in a reagent for the determination of myocardial necrosis.
- 2 Katus HA, Remppis A, Looser S, et al. Enzyme linked immunoassay of cardiac troponin T for the detection of acute myocardial infarction in patients. *Mol Cell Cardiol* 1989;21(12):1349-1353.
- 3 Katus HA, Scheffold T, Remppis A, et al. Proteins of the troponin complex. *Laboratory Medicine* 1992;23(5):311-317.
- 4 Reichlin T, Schindler C, Drexler B et al. One-hour rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. *Arch Intern Med*. 2012 Sep 10;172(16):1211-8.
- 5 Mueller C, Giannitsis E, Christ M et al. Multicenter evaluation of a 1h-algorithm in the diagnosis of myocardial infarction using high-sensitivity cardiac Troponin T. Manuscript submitted for publication, 2014.
- 6 Hamm CW, Bassand J-P, Agewall S et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST segment elevation. The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal* 2011; 32:2999-3054.
- 7 Thygesen K, Alpert JS, Jaffe AS et al. Third universal definition of myocardial infarction: the Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. *European Heart Journal* 2012;33:2551-2567.
- 8 Latini R, Masson S, Anand IS, et al. Prognostic Value of Very Low Plasma Concentrations of Troponin T in Patients with Stable Chronic Heart Failure. *Circulation* 2007;116:1242-1249.
- 9 Omland T, De Lemos JA, Christophi C, et al. Distribution and determinants of very low levels of cardiac troponin T in patients with stable coronary artery disease: The PEACE trial. *Eur Heart J* 2008;9(202):1342.
- 10 European patent 1890154 Cardiac Troponin as an indicator of advanced coronary artery disease.
- 11 European patent 1837659 Means and methods for the differentiation of acute and chronic myocardial necrosis in symptomatic patients.
- 12 Lauer B, Niederau C, Kühl U, et al. Cardiac troponin T in patients with clinically suspected myocarditis. *JACC* 1997;30:1354-1359.
- 13 Swaanenburg JC, Klaase JM, DeJongste MJ, et al. Troponin I, troponin T, CK-MB-activity and CK-MB mass as markers for the detection of myocardial contusion in patients who experienced blunt trauma. *Clin Chim Acta* 1998;272:171-181.
- 14 Giannitsis E, Müller-Bardorff M, Kurowski V, et al. Independent prognostic value of cardiac troponin T in patients with confirmed pulmonary embolism. *Circulation* 2000;102:211-217.
- 15 Herman EH, Lipshultz SE, Rifai N, et al. Use of cardiac troponin T levels as an indicator of doxorubicin-induced cardiotoxicity. *Cancer Res* 1998;58:195-197.
- 16 Stengaard C, Sorensen JT, Ladefoged SA et al. Quantitative point-of-care Troponin T measurement for diagnosis and prognosis in patients with a suspected acute myocardial infarction. *Am J Cardiol* 2013;112:1361-1366

For further information, please refer to the appropriate operator's manual for the instrument concerned, and the Method Sheets of all necessary components.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard.



Roche CARDIAC POC Troponin T

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SYSTEM

Analyzers/Instruments on which reagents can be used

GTIN

Global Trade Item Number

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Additions or changes are indicated by a change bar in the margin.

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