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Roche CARDIAC POC Troponin T cobas®

REF

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SYSTEM

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cobas h 232

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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. The Roche CARDIAC POC Troponin T Test is intended for near-patient testing.

Not for self-testing.

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 kDa) 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, heartcontusion¹³, pulmonary embolism¹⁴ and drug-induced cardiotoxicity.¹⁵ Elevated troponin in renal failure has been found to be associated with increased cardiovascular risk.¹⁶ For example, chronic cTnT elevation > 50 ng/L was detected in > 50 % patients with severe renal failure.¹⁷

Roche CARDIAC POC Troponin T allows early detection of cTnT.

In pre-hospital studies^{18,19}, 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, 924 out of 985 patients were eligible for data analysis of which 192 were later diagnosed to have AMI. A cTnT concentration \geq 50 ng/L was found in 107 subjects of whom 73 (68 %) had AMI. A pre-hospital TnT value \geq 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 these studies^{18,19}, 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.

The Roche CARDIAC POC Troponin T can be used in critical professional healthcare environments such as emergency units and ambulances.

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 2 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

User training

The operation of the **cobas h 232** instrument and the execution of the test is described in the **cobas h 232** instrument manual. No dedicated training is required.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:

Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:

Apply all relevant local disposal regulations to determine the safe disposal.

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 to be suitable: Sarstedt Monovette, Becton Dickinson Vacutainer, Greiner Vacuette, Kang Jian Heparin Tube, Gong Dong Heparin Tube.

Note: In the case of Kang Jian and Gong Dong, only tubes without separating gel have been tested.

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 (or other suitable pipettes with pipetting volume of 150 µL)
- REF 07831005190, Roche CARDIAC POC Troponin T 2-Level Control (2 x 1 mL)
- 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 \geq 03.00.02, serial number \geq KQ0120000



Roche CARDIAC POC Troponin T **cobas**[®]

- [REF] 04901142190, **cobas h 232** instrument with scanner, software version \geq 03.00.02, serial number \geq KS0210000

▪ General laboratory equipment

For Germany only:

- [REF] 07912218190, Roche CARDIAC POC Troponin T Control (2 x 1 mL)

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 or Roche CARDIAC POC Troponin T 2-Level 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.

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 (unconjugated bilirubin \leq 20 mg/dL, conjugated bilirubin \leq 10 mg/dL), hemolysis (Hb \leq 200 mg/dL), lipemia (triglycerides \leq 1000 mg/dL), haematocrit values in the range of 25-53 %, and biotin \leq 200 ng/mL.

Criterion: Recovery within \pm 15 % of initial value at troponin T concentrations \geq 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 human 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, testing 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.

No interferences of the following special cardiac drugs have been observed up to the specified concentrations:

Alpha-Lipoic acid (300 mg/L), Amlodipine (0.075 mg/L), Evolocumab (60 mg/L), Atorvastatin (0.75 mg/L), Canagliflozin (300 mg/L), Carvedilol (50 mg/L), Clopidogrel (75 mg/L), Dabigatran (525 mg/L), Digoxin (0.5 mg/L), Epinephrine (Adrenaline) (0.5 mg/L), Insulin (1.6 mg/L), Isosorbide mononitrate (2.21 mg/L), Lidocaine (20 mg/L), Liraglutide (0.168 mg/L), Lisinopril dehydrat (40 mg/L), Methylprednisolone (80 mg/L), Metoprolol (150 mg/L), Phenprocoumon (Marcumar) (15 mg/L), Propafenone (900 mg/L), Reteplase (33.3 mg/L), Rivaroxaban (40 mg/L), Sacubitril (194.4 mg/L), Spironolactone (400 mg/L), Tolbutamide (1500 mg/L), Torasemide (200 mg/L), Valsartan (205.6 mg/L), Verapamil (240 mg/L).

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

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

The Limit of Blank, Limit of Detection and the Limit of Quantification are $<$ 40 ng/L.

Expected values

The pre-hospital studies¹⁹ described in the Summary section showed the following outcome:

| Troponin T concentration | Result displayed | Comment |
|--------------------------|---|---|
| $<$ 50 ng/L | For example: Trop T $<$ 40 ng/L or Trop T 42 ng/L | Both typical and atypical symptoms in connection with a cTnT value $<$ 50 ng/L call for the application of further diagnostic measures, including repeated cTnT tests e.g. after 3-6 h to detect rising troponin T levels. ⁶ |
| \geq 50 ng/L | For example: Trop T 100 ng/L or Trop T $>$ 2000 ng/L | A cTnT value \geq 50 ng/L was highly predictive of long term mortality, irrespective of AMI. 68 % of the patients with cTnT \geq 50 ng/L had an AMI. Ensure appropriate treatment in the catheterization laboratory, an acute cardiac care unit, or another emergency facility. |

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 are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability was measured with 3 lots of Roche CARDIAC POC Troponin T test in 4 hospitals. Pooled coefficient of variation resulting from ten-fold serial testing with patient heparin blood samples were 9.3 % in the low medically relevant concentration range (40 ng/L to 200 ng/L), 11.8 % in the medium concentration range (200 ng/L to 600 ng/L) and 12.9 % in the high concentration range (600 ng/L to 2000 ng/L) of the assay. The upper one-sided 95 % confidence limit of the pooled coefficient of variation was below 11.8 % over the entire measurement range. Intermediate precision was measured with the Roche CARDIAC POC Troponin T Control in 4 hospitals. The upper one-sided 95 % confidence limit of the pooled coefficient of variation was below 11.9 %.²⁰



Roche CARDIAC POC Troponin T

Method comparison

Representative comparisons of 3 lots of the Roche CARDIAC POC Troponin T test with the Elecsys Troponin T high-sensitive test in a clinical patient population showed slopes between 0.98 and 1.09.²⁰

References

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For further information, please refer to the appropriate Operators Manual for the analyzer 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.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

The Summary of Safety & Performance Report can be found here: <https://ec.europa.eu/tools/eudamed>

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):



Device for near-patient testing



Device not for self-testing



Analyzers/Instruments on which reagents can be used



Global Trade Item Number



Unique Device Identifier

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

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