

# Increased Cardiac Troponin-T in Patients without Myocardial Infarction

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## ABSTRACT

According to the World Health Organization, the diagnosis of acute myocardial infarction (AMI) is based on two of the three main criteria: changes in the ECG (up to 25% of myocardial infarctions are not reflected in the ECG), anginous pain, and increased markers of myocardial necrosis. In 2000, the European Scientific Society and the American College of Cardiology made a correction to the definition of AMI, according to which the determining factor in the diagnosis of AMI is the detection of an increased level of specific markers of myocardial necrosis — cardiac troponins in the blood. Troponin is a protein that is part of myofibrils. Cardiac troponin contains three subunits: T, I, and C. Troponin C is non-specific for the myocardium, in contrast to the T and I subunits, whose structure in the contractile fibers of cardiomyocytes differs from similar proteins of other muscle cells. The widespread use of the determination of cardiac troponins in the blood significantly increased the detection of AMI (by 30-200%).

Until recently, it was believed that troponins enter the blood only as a result of the death of cardiomyocytes. However, in recent years, it has been shown that troponins can penetrate into the interstitial space, and then into the blood, when cardiomyocytes are damaged with an increase in the permeability of their cell membranes, which can be caused not only by AMI, but also by conditions accompanied by hyper production of pro-inflammatory cytokines (tumor necrosis factor- $\alpha$ , interleukin-1, etc.).

The aim of this study was to analyze the final diagnoses in patients with increased cardiac troponin-T levels without a clinical picture and characteristic ECG changes in AMI.

**KEYWORDS:** acute myocardial infarction, cardiomyocytes, cardiac troponin-T, anginous pain

## Materials and methods

The study included 54 patients (36 men, 18 women, aged 54 to 87 years, on average  $-69.8 \pm 11.2$ ). The inclusion criterion

was an increase in the level of cardiac troponin-T above the diagnostically significant level (more than 0.3 ng / ml). The exclusion criteria were:

- clinical picture of acute coronary syndrome (typical angina attacks);
- ECG changes characteristic of AMI on the first day of inpatient treatment (elevation or severe depression of the ST segment, the appearance of new Q waves).

All patients underwent a general clinical examination. The level of cardiac troponin-T in the blood (using the device Cardiac Reader Roche, Germany) was determined at admission, or 14-16 hours after the deterioration of the condition. ECG registration was performed on admission to the hospital and daily. Echocardiography was performed on the device GE Vivid 7 (USA) according to the generally accepted method. In addition, the level of transaminases, urea, creatinine, bilirubin, total protein, MB-CK in the blood was analyzed, gases, blood electrolyte, acid-base balance were examined. Chest radiography was performed at admission, in some cases — repeatedly. If necessary, the patients underwent ultrasound examination of the abdominal cavity and kidneys, blood culture, and brain CT.

The severity of the patient was determined based on the calculation of the SAPS II index, which assumes an assessment of the urgency of the patient's admission to the hospital, the presence of chronic diseases, age, temperature, daily diuresis, blood pressure, heart rate, blood oxygenation index (FiO<sub>2</sub>/PaO<sub>2</sub>), white blood cells, sodium, potassium, urea, bicarbonate and bilirubin, as well as an assessment of the level of consciousness on the Glasgow scale.

The final diagnosis was established on the basis of the analysis of the clinical picture, the study of the dynamics of the main symptoms, the data of a comprehensive examination, in some cases — on autopsy.

**Table 1 Mortality of patients included in the study and the level of cardiac troponin-T**

Nosological form	Total number of patients	Number of deceased patients	Troponin-T level in discharged patients (ng/ml)	Troponin-T level in the deceased (ng/ml)
AMI	22	11	0.79 $\pm$ 0.19	1.62 $\pm$ 0.21*
Septic condition	16	9	0.63 $\pm$ 0.14	1.66 $\pm$ 0.27*
Oncopathology	8	6	0.74 $\pm$ 0.49	1.49 $\pm$ 0.34
Diabetic nephropathy with CRF	4	2	0.58 $\pm$ 0.34	1.59 $\pm$ 0.58
Brain infarction	3	1	0.61 $\pm$ 0.45	1.31 $\pm$ 0.61
B12-deficiency anemia	1	1	0.49	1.69

Note. Here and in Table. 2: \* - statistical significance of differences between the level of troponin T in deceased and discharged patients ( $p < 0.05$ ).

Statistical processing of the results of the study was carried out using the program "STATISTICA 6.0". We used: the Kolmogorov–Smirnov test to assess the statistical significance of the difference when comparing the indicator of two independent groups; the Spearman test to conduct a correlation analysis. In all measurements, the arithmetic mean was used as an indicator of the average value, and the standard deviation was used for the spread indicator.

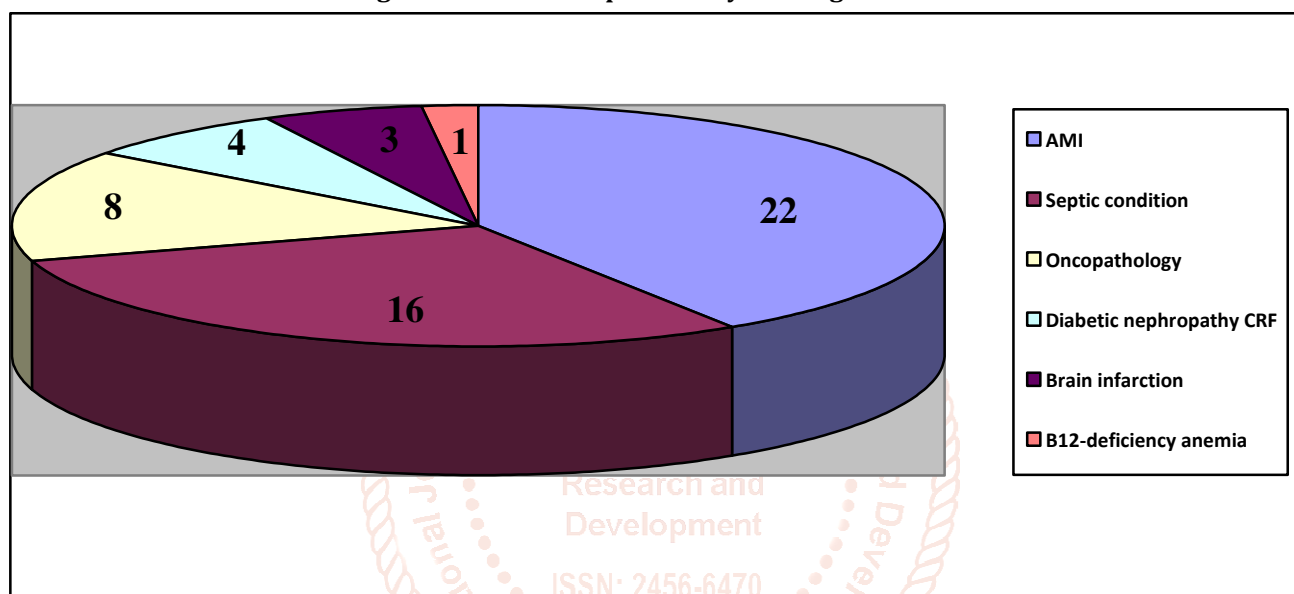
### Results and discussion

All 54 patients included in the study had manifestations of multiple organ failure: the SAPS II index ranged from 50 to 86 (an average of  $74.4 \pm 11.2$ ). 30 patients died. The level of cardiac troponin-T was in the range of 0.06-2.0 ng/ml (on average,  $1.21 \pm 0.12$ ).

In 22 patients out of 54 (40.7%), the final diagnosis was MINE. The diagnosis of AMI was made on the basis of the appearance of the characteristic dynamics of the ECG, the progression of congestive left ventricular failure. In 7 patients, AMI occurred on the background of decompensated diabetes mellitus, in 9 patients, AMI was repeated, and in 7 patients, there was repeated AMI on the background of decompensated diabetes mellitus. Of the 22 patients with AMI, 11 patients died, and the diagnosis of AMI was confirmed by autopsy.

In the remaining 32 patients, the diagnosis of AMI was not confirmed. Figure 1 and Table 1 show the distribution of patients included in the study by nosological forms.

**Fig.1 Distribution of patients by nosological forms**



In 16 patients were diagnosed with septic condition: 8 and generalized peritonitis (5-and — thrombosis in mesenteric vessels with gangrene of the bowel, 1 destructive cholecystitis, the 1st — perforation of the colon tumor, the 1st — pancreatic necrosis), 5-and — epistemology jade 2-x—destructive pneumonia, the 1st one is a common inflammation of the subcutaneous and intermuscular adipose tissue of the thigh. In 8 patients, various oncopathologies with cancer intoxication were detected (in 3-stomach cancer, in 2-lung cancer, in 1-prostate cancer, in 1 — cervical cancer). After computed tomography, 3 patients were diagnosed with a massive cerebral infarction (2-by ischemic type, 1-by hemorrhagic type with a breakthrough in the ventricles of the brain). In 4 patients, chronic renal failure was detected against the background of long-term diabetes mellitus with diabetic nephropathy (creatinine level was from 730 to 1131 mmol/l). 1 patient had severe B12 deficiency anemia (hemoglobin 59 and 64 g/l).

It turned out that the level of troponin-T in the deceased was on average  $1.61 \pm 0.28$  ng/ml, which is significantly higher than in the discharged patients ( $0.64 \pm 0.19$  ng/ml). This indicates an unfavorable prognosis of a pronounced increase in troponin-T.

The level of troponin-T in patients with AMI was practically the same as in patients with other diseases ( $1.24 \pm 0.21$  and  $1.20 \pm 0.19$  ng / ml, respectively).

Considering that the level of troponin-T was significantly higher in the subgroup of severe patients, a correlation analysis was performed between the level of troponin-T and the integral indicator of the patient's severity-the SAPS II index. A significant positive correlation was found.

In the majority of patients included in the study, the overall left ventricular contractility was reduced: the ejection fraction (EF) was in the range of 17-52% (on average,  $37.7 \pm 11.2\%$ ). The EF in patients with AMI was significantly lower than in other patients (Table 2). At the same time, the EF in those who died (from AMI and other diseases) was significantly lower than in those who were discharged.

In patients with AMI, there was no correlation between EF and the level of troponin-T, whereas in patients with other diseases, EF was inversely correlated with the level of troponin T (correlation coefficient  $-0.45$ ;  $p=0.003$ ). These data may indicate that the level of troponin may reflect the degree of cardiodepression in patients without AMI, whereas in AMI, the reduction in contractility is affected not only by the amount of necrotic myocardium, but also by other factors (hibernating myocardium, the presence of foci of fibrosis after AMI, etc.).

The present study showed that AMI is diagnosed only in 40% of patients with elevated troponin-T without a typical clinical picture of AMI. The remaining patients had another underlying disease with manifestations of multiple organ failure. It should be emphasized that all the patients included in the study were in critical condition when they were admitted. Increased levels of troponin-T correlated with the severity of the condition; in deceased patients, the level of troponin was significantly higher than in discharged patients. It should be noted that the level of troponin-T in patients with AMI and other diseases practically did not differ. There are reports in the literature that some severe diseases lead to an increase in the level of cardiac troponin-T in the blood. In the present study, an increase in cardiac troponin-T was detected mainly in patients with multiple organ failure. According to the literature data, it is multi-organ failure that leads to a "non-coronarogenic" increase in cardiac troponins in the blood: for example, Ammann P., Maggiorini M., 2003, studied the level of troponin-T in patients with sepsis without AMI. As a result of this study, it was shown that an increase in troponin-T was significantly more often detected in patients with septic shock, which is the cause of multiple organ failure, while the level of troponin-T directly correlated with the level of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6). The authors suggest using troponin-T as an additional factor in the unfavorable course of the disease in patients with a septic condition.

**Table 2 Ejection fraction depending on nosology and outcome (%)**

The outcome of the disease	Values of the ejection fraction depending on the nosology		
	AMI (n=22)	other diseases (n=32)	p
Favorable outcome (n=24)	43.1 $\pm$ 9.1	52.1 $\pm$ 10.4	0.039
Fatal outcome (n=30)	23.6 $\pm$ 8.4	39.1 $\pm$ 8.9	0.028
p	0.013	0.021	

The increase in troponin-T levels in patients without AIM identified in this study appears to be associated with myocardial damage due to a systemic inflammatory response. A systemic inflammatory reaction occurs as a result of massive cell damage due to severe hypoxemia, acidosis, endo and exogenous intoxication, as well as exposure to microbial toxins. Damaged tissues secrete a large amount of pro-inflammatory cytokines, which contribute to the infiltration of tissues by neutrophils and macrophages, activation of lipid peroxidation, and hyperproduction of nitric oxide. All these processes aggravate the existing tissue damage, leading to the formation of a vicious circle and multiple organ failure. Ut a praecessi of hyperproduction de proinflammatory cytokines ut a praecessi of a systemica inflammatione reactionem, damnum cardiomyocytes cum progressum myocardial praesent est possibile. In particulari, pro-inflammatione substantiae, agere in cellam membrana, augere permeability. Hoc posito, factum est, et probatum in 1984 per Piper et al., tunc sustinetur Wu A. H., Ford L., 1999, et confirmatum per sequens opus per Ammann P. et al., 2003. Ut a praecessi, cordis troponins soluta in intercellular spatium. Auctores explicare posse diffusio cordis troponins-T et ego per integrum membrana tam parva magnitudine moleculis his servo se (33.5 et 25.5 kDa, respective), et per eorum alia ruptio in responsione ad cellularum hypoxia. In connection with the above, it can be assumed that the increase in cardiac troponins in the blood in patients with multiple organ failure is not a false positive, but indicates the severity of the process involving the myocardium in the pathological process. This assumption is confirmed by the decrease in left ventricular EF in the majority of patients identified in this study and the inverse correlation between EF and the level of troponin-T and EF in patients without AMI. The inverse correlation between EF and the level of cardiac troponins was revealed by verElst K. M. et al., 2000. The absence of a correlation between EF and the level of troponin-T in AMI patients is probably due to the fact that some patients suffered repeated AMI, that is, they already had a decrease in myocardial contractile function.

In conclusion, we can say that, despite the cardiospecific nature of troponin-T, its detection in the blood of patients in extremely serious condition, in the absence of other manifestations of AMI, is not a specific symptom of AMI, but

indicates the involvement of the myocardium in the pathological process, which may be a manifestation of multiple organ failure with a systemic inflammatory reaction. For this reason, the detection of elevated levels of cardiac troponins in the blood of this contingent is prognostically unfavorable.

#### Literature:

- [1] Myocardial infarction redefined — a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J. Am. Coll. Cardiol. 2000; 36: 959—969.
- [2] Braunwald E., Antman E. M., Beasley J. W. et al. ACC/AHA guidelines for the management of patients with unstable angina and non ST segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J. Am. Coll. Cardiol. 2000; 36: 970—1062.
- [3] Alpert J. S., Thygesen K., Antman E. et al. Myocardial infarction redefined: a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J. Am. Coll. Cardiol. 2000; 36: 959—969.
- [4] Collins P. O., Gaze D. C. Biomarkers of cardiovascular damage. Med. Princ. Pract. 2007; 16: 247—261.
- [5] Coudrey L. The troponins. Arch. Int. Med. 1998; 158: 1173—1180.
- [6] Ammann P., Pfisterer M., Fehr T. et al. Raised cardiac troponins. B.M.J. 2004; 328: 1028—1029.
- [7] Kontos M. C., Fritz L. M., Anderson F. P. et al. Impact of the troponin standard on the prevalence of acute myocardial infarction. Am. Heart J. 2003; 146: 446—452.
- [8] Ferguson J. L., Beckett G. J., Stoddart M. et al. Myocardial infarction redefined: the new ACC/ESC definition, based on cardiac troponin, increases the apparent incidence of infarction. Heart 2002; 88: 343—347.

- [9] Guest T. M., Ramanathan A. V., Tuteur P. G. et al. Myocardial injury in critically ill patients: a frequently unrecognized complication. J.A.M.A. 1995; 273: 1945—1949.
- [10] Turner A., Tsamitros M., Bellomo R. Myocardial cell injury in septic shock. Crit. Care Med. 1999; 27: 1775—1780.
- [11] Ammann P., Fehr T., Minder E. I. et al. Elevation of troponin I in sepsis and septic shock. Intens. Care Med. 2001; 27: 965—969.
- [12] Le Gall J.R., Lemeshow S., Saulnier F. A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. J. A. M. A. 1993; 270: 2957-2963.
- [13] Wu A. H. Increased troponin in patients with sepsis and septic shock: myocardial necrosis or reversible myocardial depression? Intens. Care Med. 2001; 27: 959-961.
- [14] Wong P., Mussay S., Ramsewak A. et al. Increased cardiac troponin T levels in patients without acute coronary syndrome. Postgrad. Med. 2007; 83: 200-205.
- [15] Ammann P., Maggiorini M. Troponin as a risk factor for mortality in critically ill patients without acute coronary syndromes. Am. Coll. Cardiol. 2003; 41: 2004—2009.
- [16] Afessa B., Green B., Delke I., Koch K. Systemic inflammatory response syndrome, organ failure and outcome in critically ill obstetric patients treated in the intensive care unit. Chest 2001; 120: 1271-1277.
- [17] Matsuda N., Hattori Yu. Systemic inflammatory response syndrome (SIRS): Molecular pathophysiology and gene therapy. J. Pharmacol. Sci. 2006; 101: 189-198.
- [18] Kaye A.D., Hoover J. M., Belukh A. R. Modern review of multiple organ failure. Middle East J. 2005; 18: 273-292.
- [19] Rudiger A., Singer M. Mechanisms of sepsis-induced cardiac dysfunction of thion. Crete. Care Med. 2007; 35: 1599-1608.
- [20] Piper H. M., Schwartz P., Spar R., et al. Early release of enzymes from myocardial cells is not associated with irreversible cell damage. Cell. Cardiol. 1984; 16: 385-388.
- [21] Wu A. H., Ford L. Release of cardiac troponin in acute coronary syndromes: ischemia or necrosis? Klin. Chim. Acta 1999; 284: 161-174.
- [22] Babuin L., Jaffe A. S. Troponin: a biomarker of choice for detecting heart damage C. M. A. J. 2005; 173: 1191-1202.
- [23] Wu A. H. Increased troponin levels in patients with sepsis and septic shock: myocardial necrosis or reversible myocardial depression? Intensive Care Med. 2001; 27: 959-961.
- [24] Ver Elst K. M., Spapen H. D., Nguyen D. N. et al. Cardiac troponins I and II T-biological markers of left ventricular dysfunction in septic shock. The wedge. Chem., 2000; 46: 650-657.

