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Diagnostic Significance of Troponin in Acute Myocardial Infarction

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Summary

Introduction: Laboratory tests of cardiac markers are a standard component in the diagnosis and treatment of myocardial infarction. Cardiac troponin is widely regarded as the marker with the highest diagnostic specificity for confirming a diagnosis of myocardial infarction.

Aim: The aim of this study is to establish the diagnostic significance of troponin and to illustrate the kinetics of troponin concentration increase within 24 hours of hospitalization. Additionally, we aim to investigate the reliability of troponin determination within the first 3 hours after the onset of chest pain.

Materials and methods: This retrospective study was conducted using medical archive data from 50 patients hospitalized in the Department of Cardiology at Dubrovnik General Hospital. The patients' ages ranged from 44 to 85 years. The inclusion criterion was medical documentation confirming myocardial infarction based on clinical symptoms and other diagnostic procedures. Sample analysis was conducted at the Department of Laboratory Diagnostics using the immunochemical analyzer Architect i2000SR from Abbott (Illinois, USA).

Results: A statistically significant difference was observed between patients analyzed within 3 hours from the onset of chest pain and those analyzed more than 3 hours after the onset of chest pain. All patients analyzed more than 3 hours after exhibited elevated troponin levels. Additionally, we monitored the dynamics of troponin elevation within the first 24 hours of hospitalization.

Conclusion: This study underscores the necessity of using troponin analysis in a correct way to justify its status as a gold standard for diagnosing myocardial infarction, suggesting patients should be analyzed after at least 4 hours from the onset of chest pain.

Keywords: laboratory tests, myocardial infarction, troponin

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Introduction

Heart and blood vessel diseases are the leading causes of death and represent a significant public health concern. Today, we are addressing a global epidemic of cardiovascular diseases. According to data from the World Health Organization (WHO), in 2019, cardiovascular diseases accounted for 17.9 million deaths worldwide, representing 32% of all global deaths. Among these, 7.3 million were attributed to ischemic heart disease and 6.2 million to cerebrovascular disease[1].

Myocardial infarction (MI) is the result of heart muscle cell deterioration caused by a sudden decrease or complete interruption of blood flow through the heart's blood vessels, leading to an imbalance between the supply and the heart muscle's need for blood.

In exceptional cases, heart attacks can occur even in individuals with seemingly healthy coronary arteries due to differences in blood supply to the myocardium and its increased oxygen requirements[2].

Complications stemming from MI are not uncommon and are often complex. They depend on the degree of electrical instability and the extent of myocardial damage[3].

The clinical presentation of MI primarily depends on the location and size of the infarcted area.

In some patients, the infarction may have minimal effects, allowing them to continue their usual activities. However, this can lead to potentially dangerous consequences.

Laboratory tests of cardiac markers are a standard part of the diagnosis and treatment of myocardial infarction. These tests are particularly valuable when the electrocardiogram (ECG) findings are inconclusive. Sensitive markers are gradually released based on the degree of coronary stenosis, the development of collateral blood flow, and the severity of ischemia. Their measurement aids in diagnosing the condition, optimizing the success of reperfusion following thrombolytic therapy, identifying reocclusions and reinfarctions, determining the infarction's size, and detecting MI during cardiac or other surgical procedures[5].

Today, cardiac troponin is considered the test with the highest diagnostic specificity for the final diagnosis of MI[3].

Three decades ago, the first immunochemical tests became available in the market. Nowadays, most laboratories employ the third generation of tests, which can quantitatively measure the concentration of cardiac troponin (in units ng /mL). Since then, their utilization has been incorporated into all guidelines for the diagnosis of MI[6].

In the current guidelines of the European Society of Cardiology and the American College of Cardiology, as part of the redefinition of the diagnosis of MI, elevated troponin values are a prerequisite for diagnosing myocardial infarction and differentiating it from unstable angina pectoris within the context of acute coronary syndrome[7].

Troponin values typically begin to rise between 3 to 8 hours after the onset of chest pain. The timing may vary based on the effectiveness of reperfusion, reaching its peak between 12 to 24 hours. This elevated concentration persists for 6 to 7 days, returning to normal within 7 to 14 days. Blood samples for analysis are collected upon patient admission and then again after 6-9 hours. Elevated troponin values indicate myocardial damage, although they do not specify the mechanism of injury. Virtually all previous studies have demonstrated a positive correlation between even minor increases in troponin levels and both short-term and long-term prognosis.

Values above the 99th percentile for a normal healthy population (<0.10 ng/mL) are considered the threshold for a positive test[4].

Recommendations on two threshold values for cTnI:

1. To differentiate between healthy individuals and those with stable angina from myocardial damage in unstable angina: 0.10 -0.3 ng/mL (according to ECS criteria).
2. To distinguish unstable angina from irreversible myocardial damage indicative of MI: >0.3 ng/mL.

It is also recommended not to determine troponin concentrations within the first 3 hours after the onset of pain due to a significant number of potential false negative values.[3]

Aim

The study's objective is to assess the diagnostic significance of troponin in patients with a confirmed diagnosis of MI. It aims to determine the timeframe within which

troponin concentration in the blood increases following the onset of pain and to demonstrate the dynamics of this increase during the first 24 hours of hospitalization. Additionally, it seeks to investigate the reliability of troponin determination within the initial 3 hours of chest pain and assess whether patients may be hospitalized with a diagnosis of MI without having elevated troponin values.

Materials and Methods

Patients

This study was conducted using medical archive data from 50 patients hospitalized in the Department of Cardiology at Dubrovnik General Hospital. The patients' ages ranged from 44 to 85 years. The inclusion criterion was medical documentation confirming myocardial infarction based on clinical symptoms and other diagnostic procedures.

Materials for work

Blood samples were drawn upon the patient's emergency hospital admission, as part of routine diagnostic procedures, and at the Department of Cardiology for patient monitoring. Each sample consisted of one tube of venous blood with a volume of 8 mL.

As per the manufacturer's instructions, all samples (from patients, controls and calibrators) should be tested within 3 hours after installation on the Architect analyzer. If samples cannot be tested within 8 hours of blood collection, serum or plasma separators, clots, or erythrocytes should be separated. For this study, serum samples were analyzed within an hour of blood extraction. These serum samples were collected in Greiner Bio-One tubes with a gel separator.

Working methods

The determination of the concentration of troponin I (cTnI) was conducted using the Architect i2000SR immunochemical analyzer from Abbott (Illinois, USA).

Architect Abbott i2000sr immunochemical analyzer is an automated selective immunochemical analyzer utilizing Chemiluminescent Magnetic Microparticle Immunoassay (CMIA) technology to measure various analytes.[8]

Data processing

This study employed a retrospective descriptive method for data processing, which was performed using a personal computer. Microsoft Office Excel and MedCalc were used to organize data and calculate fundamental statistical indicators. Differences between the individual groups were assessed using the D'Agostino-Pearson normality test and the nonparametric Mann-Whitney U-test. The significance level for interpretation was set at 5% ($p<0.05$).

Results

In this study, we explored the diagnostic significance of cTnI levels in relation to the time elapsed from the onset of chest pain and how the concentration in serum changes over time. The study involved 50 patients from the Department of Cardiology at Dubrovnik General Hospital, with a gender distribution of 60% women and 40%. Demographic data are presented in Table 1.

Table 1. **Demographic data of patients**

Total number of patients	50
Gender (male/female)	20/30
Age (years)(mean±SD)	64.1±11.8
Age range (years)	44-85

In accordance with the recommendations indicating that cTnI values typically begin to rise 4 to 6 hours after the onset of chest pain and peak between 8 to 24 hours, the subjects were categorized into two groups:

1. Patients who reported to the Emergency Room ≤3 hours after the onset of pain
2. Patients who reported to the Emergency Room >4 hours from the onset of pain

Tables 2 and 3 provide additional demographic information for these patient groups, including gender, age, time of pain occurrence, and initial cTnI values.

The D'Agostino-Pearson normality test confirmed the normal distribution in the first group, while in the second group the normal distribution was rejected, as shown in Table 4.

Table 2. **First group of patients (≤3 hours from the onset of pain)**

	Age (years)	Gender	Onset of pain (hours)	1st cTnI value (ng/mL)
1	74	M	0.5	0.319
2	61	M	0.5	0.07
3	44	W	1	0.001
4	70	M	1	0.21
5	81	M	1.5	0.016
6	44	M	2	0.027
7	57	M	2	0.031
8	61	M	2	0.11
9	64	M	2	0.032
10	65	M	2	0.073
11	67	M	2	0.249
12	70	M	2	0.228
13	80	M	2	0.077
14	45	W	2	0.179
15	56	W	2	0.035
16	71	W	2	0.018
17	53	M	3	0.107
18	53	M	3	0.11
19	83	M	3	0.182
20	54	M	3	0.052
21	48	W	3	0.3
22	55	W	3	0.402
23	61	W	3	0.031
24	70	W	3	0.071
25	83	W	3	0.136
26	80	W	3	0.268
27	70	W	3	0.414

Table 3. **Second group of patients (>4 hours from the onset of pain)**

	Age (years)	Gender	Onset of pain (hours)	1st cTnI value (ng/mL)
1	52	M	4	0.02
2	65	M	4	0.059
3	78	M	4	6.97
4	47	W	4	0.05
5	62	W	4	0.01
6	79	W	4	0.583
7	74	M	5	4.18
8	85	W	5	0.393
9	47	M	6	0.25
10	54	M	6	0.854
11	55	M	6	0.12
12	59	M	6	0.764
13	60	M	6	0.3
14	64	M	6	0.263
15	75	M	6	2.892
16	57	W	6	5.861
17	75	W	6	0.94
18	51	M	10	0.768
19	55	M	12	1.736
20	68	M	12	15.031
21	76	W	12	3.476
22	83	W	12	7.8
23	63	W	16	0.698

Table 4. **D'Agostino-Pearson test**

	1st Group	2nd Group
Number of patients	27	23
Troponin and (ng/mL) (mean±SD)	0.138±0,121	2,348±3,617
95% confidence interval	0.09080 - 0.1868	0.7846 - 3.9126
P	0,1329	<0,0001

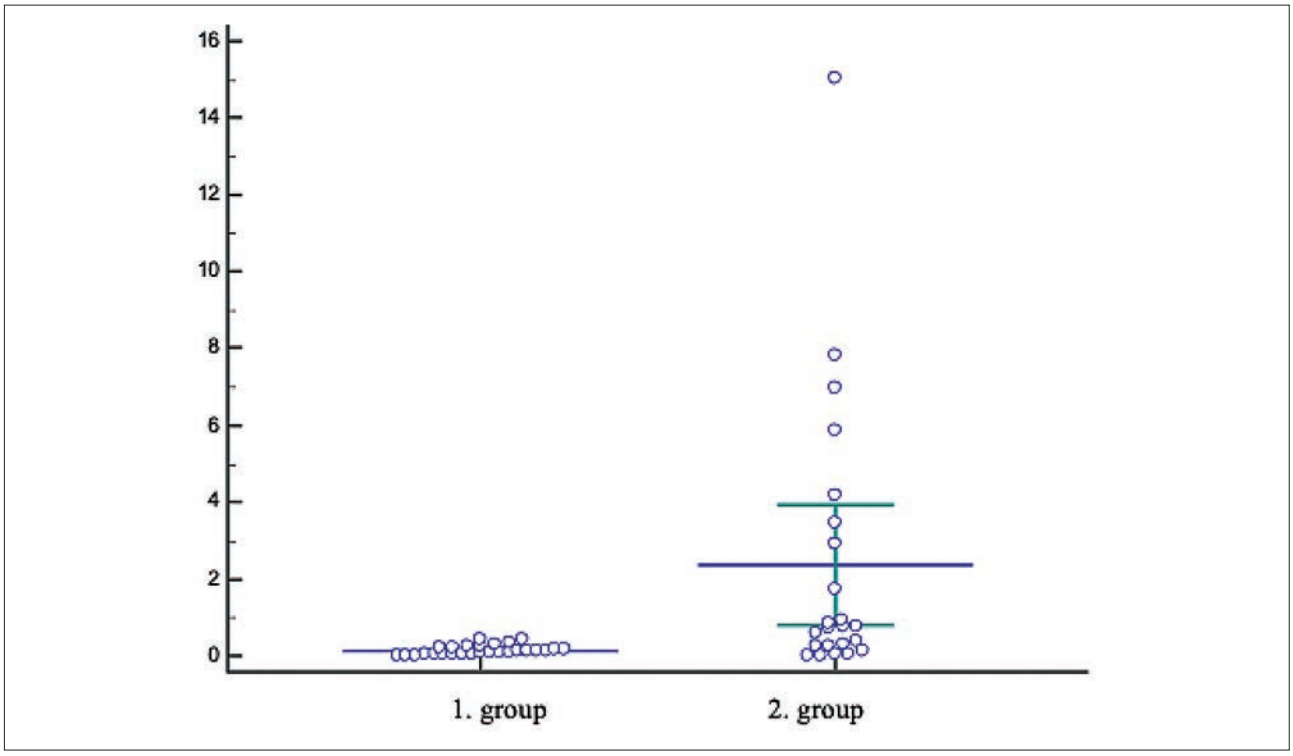

Chart 1. **Comparison of troponin concentration ranges in the first and second group**

By comparing the mean values and standard deviations of these groups, a difference was observed. This difference was confirmed using the nonparametric Mann-Whitney U-test, given the heterogenous variances in these groups. The test revealed a statistically significant difference in cTnI concentration between the groups (p=0.0001) at a significance level of P=0.05. These data, confirming the difference between the values of patients analyzed within less than 3 hours from the onset of pain and those analyzed more than three hours from the onset of pain, are presented in Chart 1.

In this study, troponin was determined once more within 24 hours from the onset of pain in 20 patients, all of whom recorded an additional increase in troponin levels. We will present the comparison of the initial and subsequent values, as well as the dynamics of troponin concentration increase in both absolute values and percentages through Table 5.

Discussion

Cardiac troponin remains the gold standard for diagnosing myocardial infarction (MI) due to its high diagnostic specificity.

Patient age range in this study was considerable, and no significance was found based on patient gender. For example, the youngest female patient, aged 44, exhibited a negative cTnI level an hour after chest pain onset, which later increased to 33,649 ng/mL in a second determination after 10 hours.

The youngest male patient was a 44-year-old who had a cTnI level of 0.027 ng/mL two hours after chest pain onset, not meeting diagnostic criteria. However, a subsequent determination after six hours yielded a value of 0.689 ng/mL, which met the diagnostic criteria according to ESC and ACC guidelines. The oldest female patient, aged 85, had a cTnI level of 0.393 ng/mL five hours after chest pain onset, meeting the WHO criteria for an MI diagnosis (>0.300 ng/mL)[3].

Table 5. **cTnI retested in first 24 hours from the onset of pain**

	1st value of cTnI (ng/mL)	2nd value of cTnI (ng/mL)	Time from the onset of pain to retesting cTnI (hours)	Increase of cTnI (ng/mL)	Increase of cTnI (%)
1	0.319	3.835	5.5	3.516	11
2	0.077	0.941	7	0.864	11.2
3	0.027	0.689	8	0.662	24.5
4	0.07	2.128	8.5	2.058	29.4
5	0.249	9.923	9	9.674	38.9
6	0.001	33.649	10	33.648	33648
7	0.21	114.209	11	113.999	542.9
8	0.016	0.384	11.5	0.368	23
9	0.25	8.319	12	8.069	32.3
10	0.94	5.697	12	4.757	5.1
11	0.11	31.642	12	31.532	286.7
12	0.11	30.502	12	30.392	276.3
13	0.402	13.344	13	12.942	32.2
14	0.035	1.165	13	1.13	32.3
15	4.18	6.633	14	2.453	0.6
16	0.3	109.217	14	108.917	363.1
17	0.031	101.743	14	101.712	3281
18	0.018	2.182	14	2.164	120.2
19	0.12	64.308	15	64.188	534.9
20	0.182	129.52	24	129.338	710.7

The oldest male patient, aged 83, had a cTnI level of 0.182 ng/mL three hours after the chest pain onset, which then increased to 129.52 ng/mL in a second determination after 21 hours.

In 54% of the patients in this study, cTnI was determined within ≤3 hours from the onset of pain, and only 11% met the criteria for confirming the diagnosis of MI (concentration > 0.300 ng/mL). These findings align with the results of other authors[9-11].

A study conducted by Bodor and colleagues showed that 16% of respondents had cTnI values >0.300 ng/mL within the first 4 hours of the onset of pain[10].

In 48% of the patients in this study, cTnI was determined >4 hours after the onset of pain, and in 78% of cases, it met the criterion for a confirmatory diagnosis of MI (concentration >0,300 ng/mL).

Similar results were reported by Jurlender and colleagues, who emphasized the high sensitivity of cTnI determination (>80%) but beyond 6 hours after symptom onset. Bodor and colleagues also reported a similar percentage of confirmatory diagnoses, at 77%[9,10].

In all patients, cTnI values increased within the first 24 hours of hospitalization, ranging from 0.6% to 33648%.

Conclusion

Considering that all patients in this study have already been diagnosed with MI, it is evident that there is considerable variation in the time and extent of troponin concentration increase among patients. Research confirms the criteria set by the WHO, which suggest that

knowledge of peak values of cardiac markers allows for a qualitative assessment of infarction size, which can influence treatment approaches. The study demonstrated the diagnostic significance of troponin measurement in MI, as all patients exhibited an increase in troponin levels within 24 hours of hospitalization.

A statistically significant difference was observed in troponin levels between the group of patients who reported to the emergency room ≤3 hours from the onset of pain and the group who reported >4 hours after chest pain onset.

This study underscores the necessity of using troponin analysis in a correct way to justify its status as a gold standard for diagnosing myocardial infarction, suggesting patients should be analyzed after at least 4 hours from the onset of chest pain.

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DIJAGNOSTIČKA VAŽNOST TROPONINA U AKUTNOM INFARKTU MIOKARDA

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Sažetak

Uvod: Laboratorijski testovi srčanih markera standardni su dio dijagnoze i liječenja infarkta miokarda. Srčani troponin smatra se markerom najveće dijagnostičke specifičnosti za konačnu dijagnozu infarkta miokarda.

Cilj: Cilj je ovog istraživanja utvrditi dijagnostičku važnost troponina i prikazati dinamiku povećanja koncentracije troponina unutar 24 sata od hospitalizacije. Dodatno, cilj nam je ispitati pouzdanost određivanja troponina u prva tri sata nakon pojave boli u prsima.

Materijali i metode: Ova retrospektivna studija provedena je upotrebom medicinskih arhiva podataka 50 pacijenata hospitaliziranih u Odjelu za kardiologiju Opće bolnice Dubrovnik.

Dob pacijenata kretala se od 44 do 85 godina. Kriterij za uključivanje bila je medicinska dokumentacija koja potvrđuje infarkt miokarda na temelju kliničkih simptoma i drugih dijagnostičkih postupaka. Analiza uzoraka provedena je u Odjelu za laboratorijsku dijagnostiku s pomoću imunokemijskog analizatora Architect i2000SR tvrtke Abbott (Illinois, SAD).

Rezultati: Utvrđena je statistički značajna razlika između pacijenata analiziranih unutar tri sata nakon pojave boli u prsima i onih analiziranih nakon više od tri sata od pojave boli u prsima. Svi pacijenti analizirani nakon više od tri sata imali su povišene razine troponina. Također, pratili smo dinamiku porasta troponina unutar prvih 24 sata od hospitalizacije.

Zaključak: Ovo istraživanje ističe nužnost ispravne primjene troponina kako bi se opravdao njegov status zlatnog standarda za dijagnozu infarkta miokarda, odnosno da bi troponin pacijentima trebao biti analiziran nakon najmanje četiri sata od pojave boli u prsima.

Ključne riječi: laboratorijski testovi, infarkt miokarda, troponin