Elevation of troponin values in differential diagnosis of chest pain in view of pulmonary thromboembolism

Određivanje vrednosti troponina pri diferencijalnom dijagnostikovanju bola u grudima sa stanovišta pulmonarne tromboembolije

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Abstract

Introduction. Acute coronary syndrome, as unstable form of ischemic heart disease, beside clinical presentation and electrocardiographic abnormalities, is characterized by increased value of troponin one of cardiospecific enzymes. Although troponin is a high specific and sensitive indicator of acute coronary syndrome, any heart muscle injury may induce its increasing, so there are some other diseases with the increased troponin value. Case report. We presented a female patient with chest pain, admitted because of suspicion of acute coronary syndrome. Performed coronarography excluded ischemic heart disease. Considering symptomatology, electrocardiographic abnormalities, increased troponin and D-dimer values, as well as echocardiography finding we considered pulmonary embolism as a differential diagnosis, which was confirmed by pulmoangiography. Conclusion. Isolated increased troponin values are not enough for diagnosis of acute coronary syndrome.

Key words: coronary disease; diagnosis, differential; pulmonary embolism; chest pain; troponin I.

Introduction

Any cross-striped muscle fiber is composed of several hundred to several thousand myofibrils, each of which contains 1,500 myosin and 3,000 actin filaments. Actin filament is composed of three different protein components: F-actin, tropomyosin and troponin (Tn). Troponin achieves its physiological role in controlling the contraction of cardiac and skeletal muscle thanks to its structure, since it consists of three loosely related protein subunits: troponin I (TnI), troponin T (TnT) and troponin C (TnC). Cardiac troponins (cTnT and cTnI) highly sensitive and specific indicators of myocardial damage, because it leads to the increase of troponins in peripheral blood only 3 to 4 hours after the necrosis of cardiac muscle cells, reaching a maximum within 12 to 24 h, and after that it returns to the initial value in 7 to 10 days (cTnI < 0.01 ngmL<sup>-1</sup> – laboratory Clinical Center Kragujevac).

In addition to troponin as markers of cardiac damage creatinine phosphokinase (CK) and its isoenzyme CK-MB
are also used, with their values increased in the peripheral blood only 8 to 12 h after myocardial necrosis. While CK-MB is highly specific for myocardial tissue necrosis, the specificity of CK is very questionable since the value of this marker rises in the necrosis of the brain, peripheral muscle and kidneys, too.5,6 Furthermore, in the detection of myocardial necrosis myoglobin plays an important role thanks to its great sensitivity (90%). However, myoglobin is not sufficiently specific because it is released from damaged heart, but from skeletal muscle and the damaged tissue, too.3,4 Similar characteristics of myoglobin are shown by a low molecular weight protein, fatty-acid binding protein (FABP)3.

It should be noted that all the above markers, with troponin in the end, belong to the late acute coronary syndrome (ACS) detectors.5 Today, more and more attention is paid to early detectors of ACS, such as leukocyte myeloperoxidase (MPO)6 or ischemia modified albumin (IMA)7, whose values rise in myocardial ischemia in the absence of myocardial necrosis, too. According to the latest research histamine plays more important role in early detection of cardiac ischemia.8

Case report

A 46-year-old female patient, was observed in the Emergency Department of Clinical Center Kragujevac, because of chest and abdominal pain, 2 hours before admission, with transitory loss of consciousness during hard physical work. The patient had been diagnosed psychosis since many years ago. At admission, the patient was afebril, tachypnoic and pale. Auscultation of the chest revealed normal breath sound with late expiratory cracks on both side from the lower parts. Initial tachycardia was registered (about 100 beats/min.) Heart sounds were normal, blood pressure was 140/90 mmHg. Other internal and neurological examinations revealed no signs of a disease.

Electrocardiogram (ECG) revealed sinus rhythm, frequency was about 100 beats per minute, ST depression horizontal type 0.5 mm in leads II, III, aVF, V5 and V6 and negative T wave in aVL (Figure 1a). Basic laboratory analyses revealed reduced values of hemoglobin (105...108 g × L⁻¹) and other results were in optimal range. Second ECG revealed significant evolution such as sinus bradycardia and ST elevations 0.5 mm in leads II, III, aVF, negative T wave in leads I, aVL, V2 i V3 with biphasic T in V5 and V6 (Figure 1b). After this ECG evolutions, although there were referent values of cardiospecific enzymes (cTnI < 0.01 ng·mL⁻¹, CK-MB 10 ng·mL⁻¹), a working diagnosis of ACS was set up. We expected elevations of cTnI and CK-MB considering appearance of pain and first laboratory analyses from peripheral blood had been taken not more than 2 h before. Double antiplateled and anticoagulant therapy was prescribed.

The surgeon was consulted since the patient had abdominal pain. Surgeon excluded acute surgery disease and prescribed H⁺ pump blockers. Repeated laboratory analyses revealed significant elevations of cTnI 0.18 ng·mL⁻¹ and CK-MB was in optimal range, so the patient was admitted to the Cardiology Department with the diagnosis of unstable angina. Performed echocardiography showed referent left ventricle (LV) systolic function, with no wall motions abnormalities and LV hypertrophy. LV was normal and right ven-

Fig. 1 – Electrocardiograms (ECG) of the presented patient: a) the first ECG; b) the second ECG
tricle (RV) was bvot borderline size (30 mm) with overload pressure at pulmonary artery and RV (42 mmHg) (Figure 2).

Repeated cTnI CK-MB analysis showed further elevations of cardiac troponin I (0.25 ng·mL⁻¹). Considering clear clinical signs, laboratory tests and ECG, the diagnosis ACS was confirmed, and urgent coronarography was indicated (Figure 3a and b). Performed coronarography showed angiographically normal lesions-free coronary arteries, and excluded ischemic heart disease. Further diagnostic procedure was directed to other diseases with positive cTnI values. Performed laboratory analyses showed significant elevations of D-dimer value (first value was 2,720 ng/mL, and repeated one 2,220 ng/mL). A new working diagnosis was set up – pulmonary embolism (PE) and confirmed by computed tomography (CT) pulmoangiography (multidetector computed tomography – MDCT) (Figure 4). Coumarin anticoagulants were introduced into the treatment to maintain international normalized ratio (INR) within the therapeutic range (2–3).

Deep venous doppler of the pelvic and lower extremity was made and the findings were normal. The patient neither used contraceptives nor gave information about the conditions that would make her lie in bed for long (recent surgery, pregnancy, extensive injuries, etc.). An additional laboratory tests confirmed the presence of elevated values of lupus anticoagulant (1.33) and the necessity of hematological and rheumatoid test was pointed to the patient. After two weeks the patient was discharged in good condition with recommendation for the appropriate therapy.

Discussion

Elevated values of cardiac troponins, with appropriate symptoms and ECG abnormalities, usually make a physician to suspect of ACS. In contrast to conventional enzymes, which have their baseline levels, cardiac troponins are virtually immeasurable in healthy individuals, so that the least damage of the heart muscle can be easily detected. The combined analysis of four studies, estimating the predictive properties of individual values of cardiac troponin I for acute myocardial infarction, found a sensitivity of 39% and specificity of 91%. Serial cTnI increased the sensitivity of 90% to 100%.

However, despite the fact that troponin is highly specific and sensitive indicator of ACS, any damage of heart muscle (and not only of ischemic etiology) may lead to its
increase: renal failure, supraventricular tachycardia, acute heart failure, pericarditis and myocarditis, PE, takotsubo cardiomyopathy, sepsis, stroke, heart contusion, heart surgery, a distinct physical exercise (eg marathon), and so on^9.

There are various mechanisms that lead to increased cardiac troponins in peripheral blood. Most often mentioned is ischemia, which, if lasts enough, leads to irreversible damage of heart muscle cells, ie necrosis. It can be caused by mechanical or dynamically narrowing of coronary arteries (pathophysiological basis of ACS)^3,^11 or a sudden overload blood pressure in the pulmonary artery (RV damage mechanism in PE)^2,^3. On the other side, repair of ejection fraction of the LV after sepsis or myocarditis, in which the values of troponin were elevated, indicate the possibility of reversible damage of heart muscle cells^2,^10. Studies show that troponins have high sensitivity in early detection of minor damage of cardiomyocytes in PE associated with RV dysfunction, but not in differentiation of cardiac from non-cardiac chest pain, because, in some patients presenting with PE, elevated troponin I concentrations above the normal range are observed, as well^9.

In our case, starting from clinical signs, ECG abnormalities as well as laboratory findings, it was logical to suspect ACS. We were directed to PE as differential possibility by cardiac ultrasound which showed a borderline dimension of the RV which is an independent predictor of mortality and non-fatal clinical complications in PE^11^ and enlarged values of D-dimer after performed coronarography, although our patient had intermediary Geneva (3 points) and low Well (0 point) score^3,^12. We should say that appearing of opposite T waves in precordial leads, was shown in our case, could be one of signs of PM^9,^13. The reported sensitivities and specificities for the diagnosis of PE of spiral CT vary (45%–100% and 78%–100%), and depend on the type of CT (single or multi-detector spiral CT). MDCT allows evaluation of pulmonary vessels down to sixth-order branches and significantly increases the rate of detection of PE in segmental and subsegmental levels^14.

Enlarged troponins values in patients with PE are present because of acute RV pressure overload, impaired coronary blood flow, and severe hypoxemia and they are independent predictors for in-hospital mortality. Limitation of pericardial expansion in the presence of dilated RV together with leftward shift of the interventricular septum appear to contribute to the diminished LV preload and resultant decreased cardiac output. Hypoxemia, systemic arterial hypotension, and cardiogenic shock may further increase the propensity to ischemic damage and pre-existing cardiopulmonary abnormalities may contribute to both the hemodynamic alteration and the risk of ischemia and infarction induced by PE^15.

**Conclusion**

Elevated values of cardiac troponins cannot absolutely indicate diagnosis of ACS, because laboratory is not a singular arbiter. Together with clinical signs, ECG evolution, coronarography and echocardiographic searching it could help in setting up the right diagnosis. If MDCT is available, then CT pulmonary angiogram can be used as the first-line imaging investigation for the diagnosis of PE.

**References**


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