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Original research article

Troponin levels in patients with stable CAD

Josef Daněk [a,*], Tomáš Hnátek [a], Martin Malý [a], Miloš Táborský [b], Jaromír Běláček [c], Jan Škvaril [a], Lenka Pospíšilová [d], Miroslav Černohous [a], Pavel Sedloň [a], Martin Hajšl [a], Miroslav Zavoral [a]

[a] Internal Clinic of the 1st Faculty of Medicine of Charles University and Central Military Hospital in Prague, Cardiology Department, Czech Republic
[b] Department of Internal Medicine I – Cardiology, Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital Olomouc, Czech Republic
[c] Institute of Biophysics and Informatics of the 1st Faculty of Medicine of Charles University in Prague, Czech Republic
[d] Department of Clinical Biochemistry, Central Military Hospital Prague, Czech Republic

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ABSTRACT

Introduction: Cardiac troponins are known as specific markers of myocardial damage. Their elevation in the serum is not always related to acute myocardial ischaemia. The increased sensitivity of diagnostic kits has resulted in an increase in the number of positive results in patients without acute coronary syndrome (ACS).

Study objectives: To determine the level of highly sensitive troponin T (hs TnT) in stable patients (without ACS) before selective coronarography (SCG) and to determine the correlation between hs TnT values and the extent of atherosclerotic damage to the coronary arteries.

Methodology: We studied a group of 251 consecutive patients with indications for SCG diagnosis. Indication criteria were stable angina pectoris, shortness of breath, newly diagnosed heart failure, syncope, and ventricular arrhythmia. Exclusion criteria were acute coronary syndrome, including unstable angina pectoris, prior cardiopulmonary resuscitation, cerebrovascular accident (CVA) within the last 6 months, and ongoing sepsis. The hs TnT value was determined before SCG (normal range, 0–0.013 μg/l). Monitored parameters included coronary angiography (70% stenosis of coronary artery diameter was considered significant coronary disease), age, gender, heart rate, and serum creatinine levels. The study included 182 patients with normal renal function and 69 patients with renal insufficiency. The results were processed using STATISTICA (version 12), StatSoft©, Inc. (2013).

Results: The average age of the studied population was 69.6 ± 10.3 years (median, 70 years); 33% of patients were women. The serum level of hs TnT for the entire population was 0.031 ± 0.091 μg/l (0.014). A positive hs TnT was noted in 133 patients. The population study group consisted of 121 patients with normal coronary arteries or with insignificant atherosclerotic disease. Significant damage involving one or more arteries was present in 130 patients. In the subgroup with significant coronary disease, we found a significantly higher hs TnT level

* *Corresponding author.*
E-mail address: josef.danek@uvn.cz (J. Daněk).
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than in the group of patients without significant coronary disease: 0.043 ± 0.125 μg/l (0.018) vs. 0.019 ± 0.018 μg/l (0.013) ($p = 0.008$) (Mann–Whitney test).

Significantly higher troponin levels were found in the group of patients with renal insufficiency than in the subgroup with normal creatinine levels: 0.057 ± 0.150 μg/l (0.023) vs. 0.022 ± 0.053 μg/l (0.012), respectively ($p < 0.05$) (Mann–Whitney test).

Conclusion: Slightly elevated serum troponin T levels are common in patients with stable coronary artery disease (CAD). We observed a significant correlation between the level of troponin and the presence of atherosclerotic damage to the coronary arteries. A significant correlation between the value of troponin and the extent of atherosclerotic damage (in terms of the number of damaged arteries) could not be demonstrated. On the basis of our findings, the absolute level of troponin T in patients with stable CAD must be interpreted with caution, especially in patients who also have renal insufficiency. Determination of basal troponin T levels in patients with stable CAD is reasonable as they may be used for comparison in case of change in a patient's clinical condition.

Introduction

Diagnosis of acute coronary syndrome is currently and primarily based on the presence of typical patient symptoms, EKG changes and alterations in the cardiospecific markers of myocardial damage [1]. In the past, the role of cardiospecific markers was less prominent. For decades, we have waited for a suitable (i.e., adequately specific and sensitive) marker of cardiomyocyte destruction. The general markers of cytolysis, ALT, AST and LDH, played limited roles in the diagnosis of ACS due to their low specificity. Creatine phosphokinase-MB (CKMB) has long been considered the gold standard for identifying disease. The specificity of the MB2 isoform is almost one hundred percent in physiological conditions. In standard practice, however, CK-MB elevation may occur even without myocardial damage (i.e., myopathy, rhabdomyolysis) [2]. The first papers describing the cardiac troponins were published during the 1960s [3]. At the beginning of the 70s, Hartshorne and Mueller published a paper dedicated to the significance of troponin in the context of cardiac contraction [3]. In the 1990s, papers were published dedicated to the use of troponins (the isoforms T and I) in the diagnosis of myocardial damage [4].

To comprehend the mechanism underlying the increase in serum troponin concentrations, it is necessary to become familiar with the structure of the cardiomyocyte contractile apparatus and the role of troponin in this system. There are 3 types of cardiac troponins found in striated muscle cells. Troponin C (TnC) functions as a binding protein for calcium ions, troponin I (TnI) inhibits the interaction between actin and myosin filaments (in case of Ca^{2+} deficiency, the binding sites are blocked), and troponin T (TnT) facilitates the binding of troponin C and I to tropomyosin. This structure (i.e., tropomyosin, TnC, TnI and TnT) is known as the troponin–tropomyosin complex (Fig. 1) [5].

The majority of troponin in cardiomyocytes is bound to the troponin–tropomyosin protein complex (92–94% TnT, 96–97% TnI); however, there is a small pool of loose TnT and TnI in the cytosol (6–8%, respectively, 2.8–4.1%). The role of this cytosolic fraction has been not satisfactorily elucidated thus far. We know that the molecular weights and immunoreactivities of cytosolic and bound troponins are identical. The cytosolic fraction is the first to be released into the circulation upon injury to the cardiomyocyte sarcolemma [7]. Thus, we detect this fraction during the early stages of Ischaemia. If ischaemia persists and cardiomyocyte necrosis occurs, proteolytic degradation of the troponin–tropomyosin protein complex occurs, which is responsible for release of the bound troponin fraction. Proteolysis in cases of extensive necrosis usually requires several days. Cardiac troponin levels are detectable in the serum throughout this time period, and elevations may persist for 5–10 days or, in extreme cases, for as long as 15 days, which represents a large diagnotic window for cardiac troponin elevation [5]. Thus, within a few days after a heart attack, the troponins are not suitable markers for subsequent cardiac injury. Interestingly, older cardiomarkers (CKMB, myoglobin) are present only in the cytosol; thus, their serum concentrations decline within hours.

Controversy exists regarding the relevance of cardiac troponins in transitory ischaemia, which results only in reversible cardiomyocyte changes. Slight increases in serum troponin levels were demonstrated in animal experiments by Feng et al. [8]. Suleiman [9] demonstrated higher concentrations of troponins in the coronary sinus in a model of stunned myocardium. Light has been shed on the issue by the work of

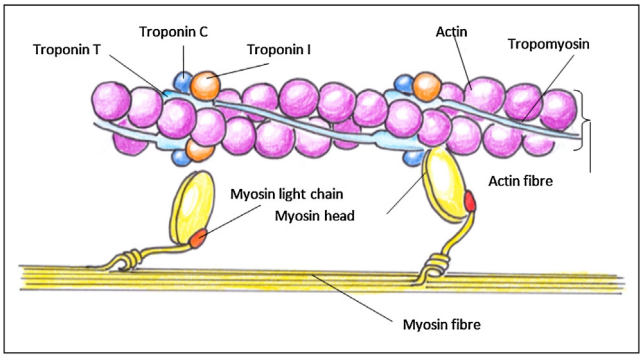

Fig. 1 – Troponin–tropomyosin protein complex, adapted by Eva Šilerová [6].