RESEARCH ARTICLE   OPEN ACCESS

Diagnostic Efficiency and Prognostic Value of Troponin T Measurement in Acute Myocardial Infarction

Merije Elezi[1*], Anila Mitre[**], Tefta Rexha[**], Besnik Elezi[***], Shpresa Memishi[***]

1.State University of Tetovo, Faculty of Food Technology and Nutrition, Gostivar, Macedonia.
2.State University of Tirana, Faculty of Natural and Mathematical Sciences, Department of Biology, Molecular Biology Section, Tirana, R. Albania, University Hospital "Mother Theresa", Albania.
2.State University of Tirana, Faculty of Natural and Mathematical Sciences, Department of Biology, Molecular Biology Section, Tirana, R. Albania.
3.State University of Tetovo, Faculty of Food Technology and Nutrition, Gostivar, Macedonia.
3.University of Tetovo, Faculty of Physical Education, Tetovo,Macedonia.

Abstract
The diagnosis and prognosis of patients hospitalized with acute myocardial ischemia is quite variable. We examined the value of serum levels of cardiac Troponin T, serum CK-MB levels for detection of ischemic myocardial injury and risk stratification within 40 days in patients with acute myocardial ischemia with one specimen taken 2-8 hours of the onset of symptoms.
Methods
We studied 141 patients with a diagnosis of acute ischemic myocardial injury. The concentration of TnT and CK-MB is made on Coobas 6000 by a electrochemioluminescence and turbidometric methods.
Results
The median duration of the ischemic episodes qualifying the patients for the study was 4 hours. Chest pain was continuous in 51.8% and intermittent in 48.2%. Troponin T levels were elevated in 47 % of the patients whose ischemic symptoms had lasted more than seven hours (p= 0.06). 33% of the patients had the elevated troponin T level but CK-MB level was normal. Mortality within 40 days was significantly higher in these patients than in patients with lower levels of troponin T. The troponin T level was variable and most strongly related to 40-day mortality (chi-square=23, p<0,001) followed by CK-MB (chi-square=10, p=0,005).
Conclusions
The cardiac troponin T level is a powerful, independent risk marker useful in the diagnosis of infarction and in the identification of patients at increased risk of mortality and morbidity.

I.   Theoretical data

Patients with acute myocardial ischemia syndrome who appear in the hospital represent a continuity of the disease from unstable angina to acute infarct. The duration, frequency and timing of the symptoms are important to make a long-term prognosis and can be used to determine the degree of unstable angina; however, these are not predictors of serious cases such as death, stroke, heart failure or ventricular arrhythmia. An ECG and serum markers are the most important objective indicators of short-term risk in these patients. Over 90% of patients with prolonged episodes of ischemia and an increase of ST segment suffer from myocardial infarction. During the absence of the ST segment, it is difficult to distinguish a difference between unstable angina and acute infarct. Some patients have an early increase of creatine kinase MB (CK-MB) which indicates a myocardial infarction, or a poor prognosis.

Currently, biochemical diagnosis of acute myocardial infarction (AMI) is confirmed by observing serial measurements of CK and CK-MB. Although measurement of these enzymes should be evaluated, both have deficiency because both enzymes are present in other tissues as well besides myocardium. Confusion exists especially when the liberation of CK and CK-MB is minimal. Diagnostic value of CK-MB has been discussed for decades and two new markers have been developed for the detection of cardiac damage. In patients with damaged acute myocardium when compared with CK-MB, cardiac troponin T and I offer specificity and sensitivity for the detection of cardiac damage.

Troponin T, the complex regulatory protein that connects the tropomyosin located in the contractile device by the myocytes of the heart, is a sensitive and special pointer in identifying cardiac necrosis. Studies on levels of troponin T measured during 24 hours have revealed increased cardiac events in patients with high levels of troponin T even without having high levels of CK-MB.

II. Goal

TnT value in the diagnosis and prediction of situations in patients with acute myocardial infarct syndrome.

Methods: For our study, 200 patients were selected with a previous diagnosis of angina pectoris that asked for help at the Emergency Clinic at the University Hospital Center of Cardiology. 141 patients qualified for the criteria of acute myocardial infarction and are the subjects of our study. 69% of the patients included in this study are males. Their age varies from 53-78. 25.8% of the patients have had a history with infarct. The study comprised a starting point for each patient from the moment they entered the emergency hospital, their progress and the end point after 40 days. During this period, different situations were evaluated for each patient, such as, infarct, repeated infarct, surgical bypass, death, etc. The final point of the study was the situation after 40 days.

The first blood sample for biochemical analysis obtained was done immediately after making an electrocardiogram and capturing of the abnormal ST segment. The blood sample was obtained with gel tubes. The analysis of TNT and CK-MB was performed within 2 hours from the collecting of the material in the clinic Intermedika in Tirana. The centrifugation was done within 10 minutes with 3000xg. The cardiac Troponin T was analyzed through the electrochemioluminescence technique in the device Coobas 6000, whereas CK-MB was analyzed in the same device through the method of turbidimetry. The reference values for Troponin T and CK-MB are from 0-14pg/ml and <25U/L, respectively.

In the first step the patient's samples (serum) is mixed with the antibody reagent that contains the biotinylation T and T Troponin - specific antibody labeled with ruthenium in the test tube . During incubation, which lasts nine minutes, T - Troponin captures antibodies present in the sample . In the second phase microparticles are added, covered with paramagnetic streptavidin. During the this phase of incubation, which lasts additional nine minutes, biotinylated antibodies were attached to surfaces covered with streptavidin microparticles. After the second incubation, the mixture that keeps immune complexes is transported to the measuring unit. Immune complexes captured on magnetic alloy electrode and reagents can be washed and removed from the reaction. In ECL reaction, conjugate is ruthenium derivative which on chemioluminiscence reaction, is electrically stimulated to produce light . The amount of light produced is proportional to the amount of the sample T Troponin. Evaluation and calculation of concentration in the sample T Troponin done through the calibration curve , which is

prepared using standard antigen with known amounts recommended by the company Roche (ST 1230) .
CK - MB were analyzed through the same device with the method of turbidimetry. The data obtained were subjects to statistical analysis. We made a statistical correlation coefficient calculating the ranks of Spearmanit and Chi - square test .

III. Results

Out of 200 patients originally included in the study , 59 did not meet the criteria of myocardial infarct, and 141 patients remained in the study . The duration of ischemic episodes is an average of 4 hours.

Chest pain was continuously in 51.8 % of cases and 48.2 % were interrupted from it. Troponin levels were increased in 47 % of patients whose symptoms lasted more than 7 hours ($p = 0.006$). Troponin T levels were rising faster than the level of CK - MB . Further on, the results obtained were divided into three groups , the first group in which T troponin levels were above the norm, reared moderate, but CK - MB values are in the norm . This is a group in which the increase of T Troponin comes as a result of the formation of thrombi in destroyed arteriosclerotic plaques. The formation of thrombi increases levels of cardiac troponin. This is due to the destruction of the left artery circulation. The second group of patients are those who have increased levels of TnT , but have normal levels of CK - MB . In this group, the ST segment levels obtained from EKG is confirmed through IM . In this group the determination of the value of TnT emerges, which is able to detect infarct even when other parameters are unchanged. In the first two groups, 33 % of individuals that participated in the study take part in the group. If Troponin analysis was not performed this group, it would not be identified . The third group of patients are those who have increased levels of TnT as well as the CK - MB . In three groups, we applied the calculation of the correlation coefficient for the level of Troponin Spearmanit T and CK - MB . By doing these calculations, it was concluded that in severe myocardial infarct, Troponin T has correlation with CK - MB ($r = 0954$ and $p < 0.01$) , while in the two previous groups, this correlation does not exist $P = 0.244$. From the study of Troponine levels measured and the patient's progress realized through the following case histories of patients that participated in the study, it was confirmed that there was a connection between the right level of adult T troponin and mortality within 40 days. in patients and progress realized through the following case histories of the patients received the study it was found that there is a connection between the right level of adult T troponin and mortality within 40 days . Patients who have increased levels of CK - Mb and TnT have a worse prognosis than those who have an increased

level of either . The relationship between levels of Troponin and closing point was studied after 40 days : 13 % death 65 % heart attack, 10 % vascularisation and the rest of the patients had no events . Troponin T levels at the time of registration predicted mortality rates within 40 days . T troponin level is the most strongly associated variable with mortality within 40 days (Chi - square = 23 , p < 0.001) followed by CK - MB level (Chi - square = 10 , p = 0.005) . Even among patients with acute ischemia with increased value of CK – MB, T Troponin was associated with high mortality rate within 40 days . Percentage of deaths or repeated cardiac infarct after 40 days were higher in patients with adult T troponin than in those with normal Troponin T (10.2 % versus 2.8 % the normal Troponin T , P < 0.001) . The level of troponin T is an important marker in the diagnosis of myocardial infarct and prediction of mortality . In other studies of this type, the serial level of Troponine T was assessed[10, 11] , while we examined a sample only taken about 2-8 hours after the onset of symptoms . High mortality in patients with adult T Troponin in obtaining this moment may reflect the influence of three factors:

- These patients have had heart attacks, which began early. Patients who have more than 6 hours of ischemic symptoms have a higher mortality rate than those presented earlier[12,13.]   T Troponin level begins to rise about an hour after the onset of symptoms and sensitivity reaches 50 % within 3-4 hours [10, 14.]

- These patients may have had short symptoms of myocardial infarct (interpreted as unstable angina and repeated infarct mortality is greater than that by a single stroke)[15.]

- Patients who die may have had major heart attacks . Large heart attacks may have caused considerable and early release of Troponin thanks to T , saturation of mechanism clearance and rapid emergence of T Troponin circulation[16, 17.]

IV. Conclusion

Our study confirms that even small levels of Troponin T are available in the diagnosis of myocardial infarct and T troponin level measured 2-8 hours after the onset of symptoms, which provides information on the identification of patients with increased risk of danger and death.

Literature

[1] Califf RM, Mark DB, et al. *Importance of clinical measures of ischemia in the prognosis of patients with documented coronary artery disease*. J Am Coll Cardiol 1988; 11:20-6.

[2] Betriu A, Heras M..; Unstable angina: *outcome according to clinical presentation*. J Am Coll Cardiol 1992; 19:1659-63.

[3] Lee TH, Rouan GW,et al. *Sensitivity of routine clinical criteria for diagnosing myocardial infarction within 24 hours of hospitalization*. Ann Intern Med 1987; 106:181-6.

[4] Karlson BW,Herlitz J, ..,et al. *Erly prediction of acute myocardial infarction from clinical history, examination and electrocardiogram in the emergency room*. Am J Cardiol 1991;68:171-5

[5] Adams JE III,Bodor GS,Davila-Roman,…et al. *A marker with high specifity for cardiac injury.* Cirkulation 1994;89:1447-8.

[6] Wu AHB, Feng YJ, …et al. *Comparison of myoglobin, creatine kinase MB, and cardiac troponin I for diagnosis of acute myocardial infarction*. Ann Clin Lab Sci 1996;26:291-300.

[7] Katus HA, Remppis A, …et al. *Diagnostic efficieency of troponin T measurements in acute myocardial infarction*. Circulation 1991; 83:902-12.

[8] Hamm CW, Ravkilde J,… et al. *The prognostic value of serum troponin T in unstable angina*. N Engl Med 1992;327:146-50.

[9] Seino Y, Tomita Y,…et al. *Early identification of cardiac events with serum troponin T in patients with unstable angina*. Lancet 1993; 342:1236-7.

[10] Katus HA, Remppis A,…et al. *Diagnostic efficiency of troponin T measurements in acute myocardial infarction*. Circulation 1991;83:902-12.

[11] Zabel M, Holnloser SH,…*Analysis of creatinine kinase, CK-MB, mioglybin, and troponin T time-activity curves for early assessment of coronary artery reperfusion after intravenous thrombolysis*. Circulation 1993;87: 1542-50.

[12] Fibrinolytic Therapy Trialists,(FTT) *Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction*. Lancet 1994;343:311-22.

[13] THE LATE Investigators. *Late Assessment of Thrombolytic Efficacy (LATE) study with alteplase 6-24 hours after onset of acute myocardial infarction*. Lancet 1993;342:759-66.

[14] Wu AHB, Valdes R Jr,…et al. *Cardiac troponin-T immunoassay for diagnosis of acute myocardial infarctio*n . Clin Chem 1994; 40: 900-7.

[15] Ohman EM, Califf RM, et al. *Consequences of reocclusion after successful reperfusion therapy in acute* yocardial infarction Cirkulation 1990;82:781-9.

[16] Wagner I, Mair J,…et al. *Cardiac troponin T relase in acute myocardial infarction is associated with scintigraphic estimates of myocardial scar*. Coron Artery Dis 1993;4;537-44.

[17] Van Dieijen Visser MP, Kragten JA,…et al. *Quantifification of Troponin T relase in plasma after acute myocardial infarction*. Ned Tijdschr Klin Chem 1995; 20-120.