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VARIATIONS OF SOME MYOCARDIC CITOLIZATION ENZYMES IN ACUTE MYOCARDIC INFARCT

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***Key words**: TGO, LDH, CK-MB enzymes, myocardial cytolysis, myocardial infarction, monitoring*

INTRODUCTION

Atherosclerotic cardiovascular disease (ACD) is a chronic disease that develops insidiously throughout life and usually progresses to an advanced stage before the onset of symptoms. It remains the leading cause of premature death in Europe, although mortality from BCV has declined considerably in recent European countries.

It is estimated that over 80% of ACD deaths currently occur in developing countries. ACD causes major disabilities: Over the next decades, years of disability loss (DALYs) are estimated to increase from a loss of approximately 85 million DALYs in 1990 to a loss of approximately 150 million DALYs globally in 2020, thus remaining the somatic cause. main productivity loss (*Graham I, Atar D, Borch-Johsnsen K., 2012*).

Cardiovascular disease is closely correlated with lifestyle, especially with tobacco use, unhealthy eating habits, sedentary lifestyle and psychosocial stress.

The World Health Organization (WHO) said that over three quarters of all deaths caused by ACD could be prevented by appropriate lifestyle changes. ACD prevention, remaining a major challenge equally for the general population, politicians and those working in the health system, is defined as a set of coordinated actions, at public and individual level, in order to eradicate, eliminate or minimize the impact. cardiovascular diseases and the disabilities that accompany them.

Atherosclerotic cardiovascular disease, especially CHD (coronary heart disease), remains the leading cause of premature deaths worldwide. ACD also affects men and women; of all deaths under the age of 75 in Europe, 42% are due to BC in women and 38% to men.

It is important to note the accumulation of evidence in recent decades that the increased cardiovascular risk occurs at (very) young ages. Even prenatal exposure to risk factors can influence cardiovascular risk throughout life (*Pop D, Zdrenghea D, Cişmaru I., 2014*).

MATERIAL AND METHODS

Blood samples needed for paraclinical investigations of acute myocardial infarction were collected from 62 patients, both male and female, during the period January-December 2018, within the Cardiovascular Diseases Institute "Prof. Dr. George I. M. Georgescu " Iasi. Because the patients were urgently addressed, the blood samples were taken at the time of presentation, as well as in the morning, *a jeun*.

To determine the biological parameters were used: compact clinical chemistry analyzer, fully automatic RX IMOLA (fig. 1) and BIOLIS 24I, the smallest clinical chemistry analyzer with the largest menu (fig. 2).

The following enzymatic biochemical parameters in serum were determined and interpreted:

- **CK-MB** (creatine kinase isoenzyme MB), the myocardial fraction of creatinine kinase associated with myocardial infarction, useful for estimating the size of the necrosis area.
- **TGO** (oxalic glutamate transaminase or aspartate aminotransferase - AST), an enzyme found in high concentrations and in the myocardium; Increased levels of AST also occur in myocardial infarction;
- **LDH** (lactate-dehydrogenase); the intracellular enzyme widely distributed in the body, being encountered also in the myocardium; Although LDH increases are nonspecific, this test is useful to confirm the diagnosis of myocardial infarction.

RESULTS AND DISCUSSIONS

Out of a total of 1028 patients admitted to AMI (acute miocardic infarct), 310 of them are women and 718 are men. Men patients represent 70% of the total number of patients admitted during this period (fig. 3). Male gender is a risk factor in coronary heart disease, the high percentage of men (70% versus 30% of women), is confirmed by reference studies conducted in this domain. Patients were divided into age samples (figures 4, 5):

- **Group A** includes very young patients, 12 patients between the ages of 25 and 39, all men.
- **Group B** includes patients between the ages of 40 and 49, eight men and two women.
- **Group C** is made up of ten patients between the ages of 50 and 59, nine of them women and one man.
- **Group D** has ten patients between the ages of 60 and 69, six women and four men.
- **Group E** comprises ten patients, four male and six women between the ages of 70 and 79 years.
- **Group F** is made up of ten patients between 80 and 95 years old, four men and six women.

Fig. 1. RX IMOLA clinical chemistry analyzer

Fig. 2. BIOLIS 24I clinical chemistry analyzer

From figure 4 we can see that AMI appears from a very young age (group A and group B). In young patients, the appearance of AMI is due to: hereditary factors (family history of coronary heart disease), unbalanced lifestyle, stress, smoking, drug use and energizing. Family aggregation of myocardial infarction cases illustrates the role of genetic factors. Descendants of those who have had a heart attack under the age of 50 have a risk of 3-5 times higher than those from families without a history of heart attack.

In the case of men, the maximum number of patients is in the age group D (60-69 years). The increased incidence of AMI in the age group 60-69 is explained by the following risk factors: (high blood pressure diabetes, obesity, smoking) and the atherosclerosis process which is directly proportional to the age. The incidence and prevalence of AMI increase progressively with age, illustrating the slow progression of coronary atherosclerosis. The 40-49 age group represents about 50% of the maximum number of patients in the 60-69 age group. Patients are of various age categories, with the youngest patient being 25 years old and the oldest being 95 years old, both of whom are male (fig. 4).

In the case of women, from figure 5 it is observed that: in the age category 30-39 years, there was no case of AMI; AMI appears in a relatively low percentage in the 40-49 age group; the maximum number of patients is 70-79 years old.

Of the 62 patients, the situation of hospitalizations by calendar months is as follows (fig. 6). In the winter months, January and February, the highest incidence of acute myocardial infarction is recorded. The spring and autumn months have about the same number of hospitalized patients. January is the month with the most cases of AMI, vasoconstriction at the coronary level due to the low temperatures, being one of the reasons, as well as the non-observance of diet and medication regimes during the winter holidays, which contribute to this balance.

The biochemical indicators followed in emergency, from the moment of hospitalization and throughout the hospitalization are the enzymes of myocardial cytolysis (CK-MB, TGO, LDH). These indicators are monitored dynamically, following the evolution of myocardial infarction, the degree of severity and the prognosis for the next period. As a result, myocardial cytolysis enzymes are represented dynamically by age group.

The graph in Figure 7 represents the evolution of MB creatinine kinase (CK-MB) during the hospitalization period in patients in age group A (25-39 years).

The maximum normal value of CK-MB is 25 U/L. Of the 12 patients, all male, 11 had CK-MB increases. The number of determinations is between two and seven for each patient, depending on the evolution, the time of hospitalization and the length of hospitalization.

The lowest values of CK-MB represented on the graph are (16 U/L, 8 U/L) in *patient no. 12 A*, being within normal limits. He is the youngest hospitalized patient with recent myocardial infarction (25 years), diagnosed with electrocardiography and coronary artery disease. He did not show up in a hospital unit in a timely manner; at the time of admission to the Institute of Cardiovascular Diseases,

myocardial cytolysis enzymes were in normal parameters.

The highest values were recorded in *patient no.8 A* (39 years), with maximum values of 936 U/L (fig. 8), the value at admission being 257 U/L (seven hours after the onset of pain).

The maximum value was recorded 12 hours after the onset of the infarction, the values registering a progressive decrease after stent implantation (466 U/L, 129 U/L, 28 U/L, 22 U/L). The patient is known to have important cardiovascular pathology (three previous infarcts, three implanted stents), high blood pressure and metabolic syndrome. Myocardial cytolysis enzymes that are monitored together with CK-MB are TGO and LDH.

The TGO values change simultaneously with the evolution of CK-MB, having values lower than this enzyme, the maximum being recorded 12 hours after the infarction (623 U/L). Lactate dehydrogenase (LDH) in IMA increases after 8-12 hours after onset, having maximum values after 24-72 hours. Normalization of values occurs in 10-14 days. The first determination is a moderately modified value, following significant increases in values, 30 hours after the onset of infarction reaching the maximum value.

The patient was made 7 determinations of myocardial cytolysis enzymes during hospitalization, each determination including the three CK-MB, TGO and LDH indicators. From the graph below we can observe the concomitant evolution of TGO and LDH, following the same route of value increases and decreases (fig. 8). CK-MB has the highest value at 12 hours from the onset of the infarction (37.4 times the normal value), TGO has the maximum value also at 12 hours (16.8 times the normal value). LDH registers a maximum level 30 hours after the onset of infarction (6.3 times the normal value), but it is the enzyme with the slowest evolution towards normalization.

CK-MB is the short-term increased myocardial necrosis enzyme, but normalizes within 4-5 days after the onset of stent-treated coronary angioplasty. The graph in Figure 9 represents the dynamic CK-MB values of the patients with IMA from **group B** aged 40-49 years. This category includes eight male and two female patients. The lowest values are recorded in *patient no. 2B* (CK-MB 14 U/L), who was admitted to hospital for serious angina pains. The patient, 49 years old, did not show enzymatic dynamics during the hospitalization period. The electrocardiogram shows previous acute myocardial infarction, coronarography confirms the diagnosis of infarction, the patient is stent with very good result.

Patient no. 7B, 45 years old at the hospital, registers the highest values of CK-MB (37 U/L at the hospitalization, the maximum value at 20 hours from the beginning-620 U/L), and then gradually decreases in five days (93 U/L, 48 U/L, 30 U/L and 20 U/L). The maximum level is 18.4 times higher than the normal level. The patient presents as risk factors hypertension and obesity grade II. The evolution was good after the implantation of the stent, without the appearance of complications (fig. 10). The TGO dynamics has the same evolution as the CK-MB, the maximum values are recorded in the second determination, 20 hours after the onset of the infarction, the maximum TGO level being 667 U/L (20.7 times higher than the maximum value accepted). LDH levels have significant increases, the second determination is 3799 (8.25 times higher than the normal value). The decreases take place gradually, maintaining high even when discharged (fig. 10).

Patient no. 3B, 47 years old, shows a slight enzymatic increase (CK-MB 29 U/L), but also a significant increase of Troponin I = 1.37 ng / ml (normal values <0, 06 ng / ml). The patient benefited from coronary imaging and stent implantation with favorable evolution. The rest of the patients have a similar enzymatic dynamics, with maximum values between 12-24 hours after the onset of the infarction and normalization of the values in 4, 5 days after hospitalization.

The graph in Figure 11 represents the CK-MB dynamics in **group C**, patients aged 50-59 years. The patients are nine women and one man patient. All patients have increases of CK-MB, the minimum values are presented by *patient no. 5C*, the highest values are recorded in *patient no.7C* (Fig. 12).

In most patients, the enzyme level is maximal at 20-24 hours after the onset of infarction, except the *patient no.5*, which was addressed 48 hours after the onset of pain, with a slightly increased value of 34U / L. The highest levels of CK-MB are presented by *patient no.7C*, 56 years old, high smoker, with known diagnoses of autoimmune thyroiditis and type 2 diabetes (fig. 12). At admission, the patient was hemodynamically stable, with electrocardiogram suggestive of IMA (ST elevation in the anterior territory) and CK-MB 33U / L (4 hours after pain onset). Emergency coronarography was performed, which confirmed acute myocardial ischemia and a metal stent was implanted on the anterior descending coronary artery.

The maximum CK-MB value of 856 U/L is 14 hours after the onset of infarction and is 34.24 times higher than the maximum allowed level. During the hospitalization period (seven days), the enzyme levels have a downward path, reaching normalization on the last day (21 U/L). The maximum TGO level is 693 U/L (18.72 times higher than the maximum allowed threshold), and the LDH has the maximum value of 3028 U/L (6.58 times the normal maximum level). TGO has a linear decrease with CK-MB, reaching normal values, LDH decreases gradually, but with a still increased value on the seventh day after acute infarction (1262 U/L).

Group D includes patients between the ages of 60-69 (fig. 13), two males and eight females. There are significant increases of CK-MB, the majority having values above 300 U / L, the highest being recorded in *patient no. 4* (766 U / L). Patient no.9 has the lowest value (31 U / L). To all other patients maximum values are recorded at the second determination of the enzyme, approximately 12-30 hours after the onset of the infarction, with the progressive decrease of the values at the subsequent determinations.

Patient no. 4D male (fig. 14), 62 years old, hypertensive, smoker, presents 11 hours after the onset of a major angina crisis. The electrocardiographic aspect is of the previous IMA, the CK-MB value at admission being 505 U/L. The maximum level is reached 24 hours after the onset of the infarction, CK-MB is 766 U / L (31 times higher than the maximum allowed value). Emergency coronarography is performed, with pharmacologically active stent implantation.

Significant increases in TGO and LDH in this patient are recorded within the first 24 hours after onset of infarction, TGO value is 880 U/L (23.8 times higher than the upper limit) and LDH of 2766 U/L (6 times higher than the normal maximum value). The decrease occurs gradually in the five days of hospitalization, the myocardial cytolysis enzymes registering modified values and upon discharge (CK-MB = 45 U/L, TGO = 109 U/L, LDH = 1387 U/L).

In **group E** (fig. 15) there are patients between the ages of 70-79 years, six females and four males. All show increases of CK-MB over the upper limit, the highest levels are recorded in *patients no.3, no.6* and *no.4* (700 U/l, 593 U/L and 540 U/L). The lowest values are found in patient no.5 (33 U/L). *Patient no. 3E* (fig. 16), 73 years old, who has been neglected for therapy, is addressed to the institute at 8 hours after the onset of a major angina crisis, expression of an antero- extensive STEMI, electrocardiographic. At admission CK-MB has the value of 157U/L, at 16 hours after the onset of pain the level increases to 700 U/L (28 times the maximum normal value). The patient benefits from coronary artery disease, which shows total acute thrombotic occlusion on the anterior descending artery, with stent implantation.

All myocardial cytolysis enzymes have high values, TGO has a maximum value of 621 U/L (16.7 times higher than the maximum allowed value), 14 hours after the onset of infarction. The curve follows the same ascending and then descending route with the CK-MB route. LDH has a maximum value of 3756 U/L (8.2 times the maximum normal value), is maintained at elevated levels between determinations 2-5, and then decreases progressively.

The graph in Figure 17 represents the CK-MB dynamics during hospitalization in patients between 80 and 95 years of age, group F. Of the ten patients, four are male and six are female. *Patient no.1F*, 95 years old, has enzymatic dynamics with high values (CK-MB at admission 284 U/L, 372 U/L at 18 hours after the onset of infarction, then with values that decrease progressively, 104 U/L, 58 U/L, 51 U/L, 49 U/L, 32 U/L). The patient was treated conservatively, with good progress, refused angiographic examination.

The highest values of CK-MB are presented by *patient no. 3F* (fig. 18), 83 years old (on admission CK-MB 31 U/L, 490 U/L at 23 hours after the onset of pain, with decreasing values in the next five days after admission, 233U/L, 91 U/L, 40 U/L, 36/L). Coronarography was performed, which objectified acute thrombotic occlusion on the right coronary artery and stent was implanted with very good result. All patients in this age group show significant increases in myocardial cytolysis enzymes.

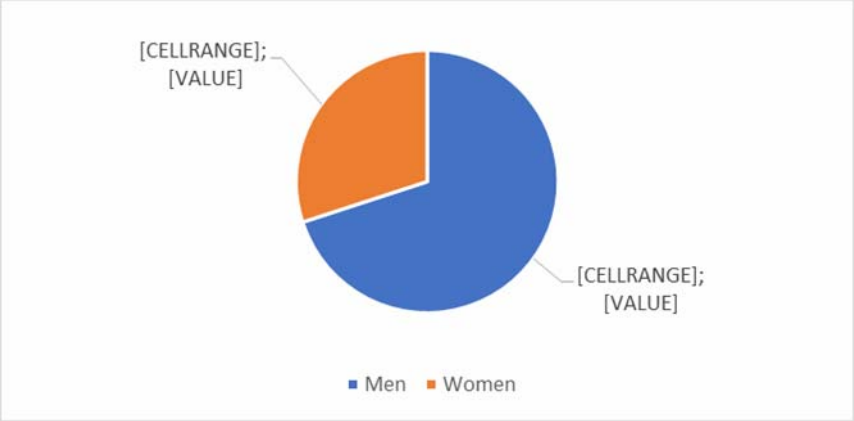

Fig. 3. Distribution of patients by sex

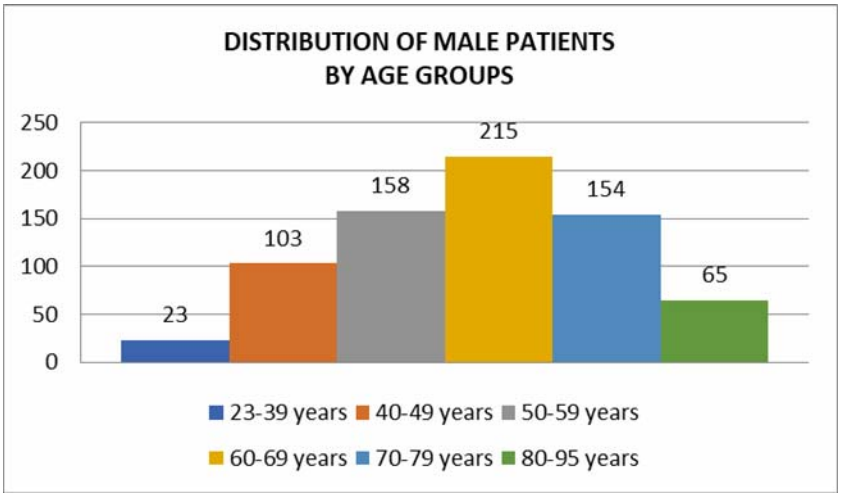

Fig. 4. Distribution of male patients by age groups

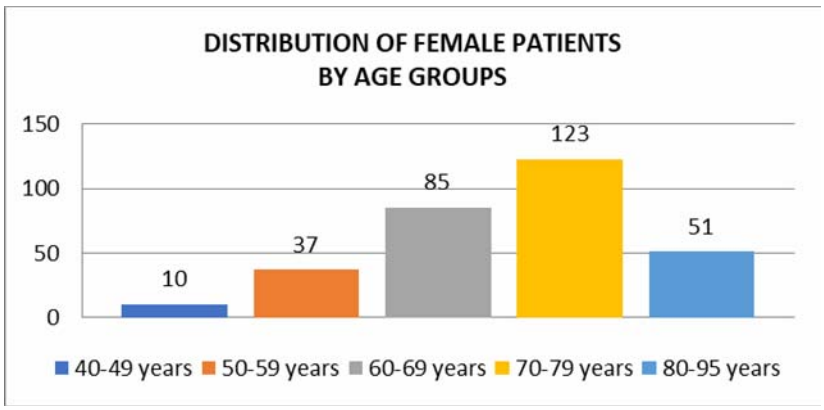

Fig. 5. Distribution of female patients by age group

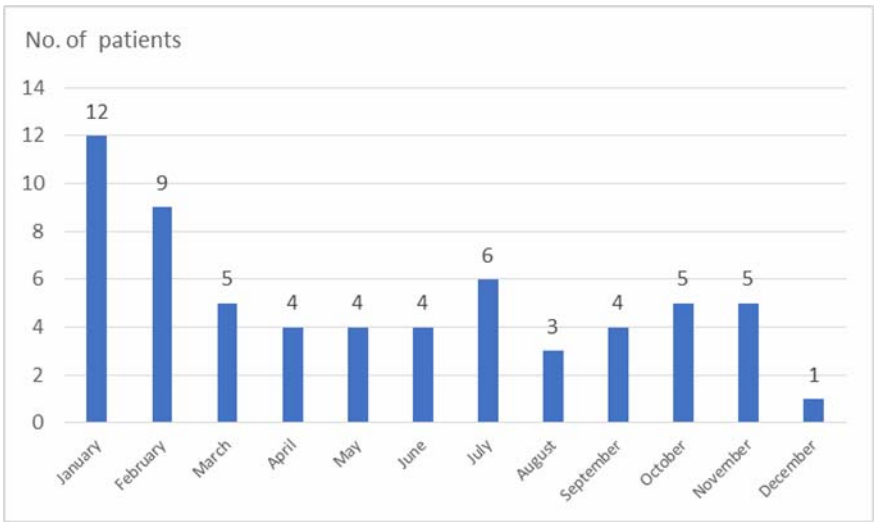

Fig. 6. Distribution of patients by calendar months

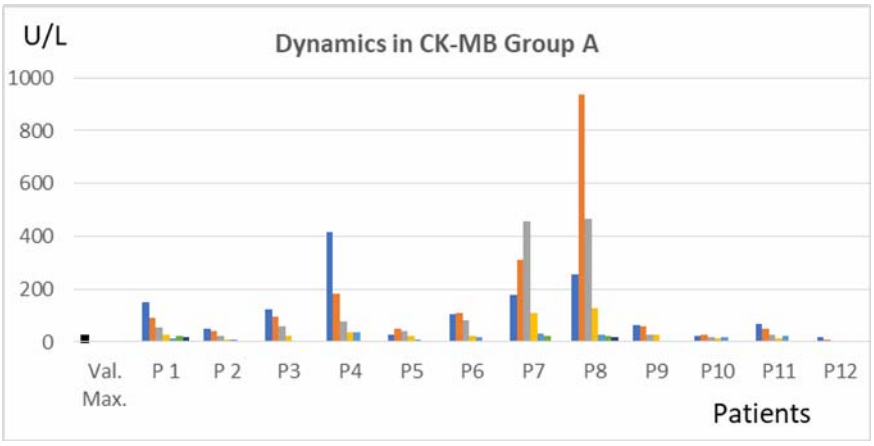

Fig. 7. Dynamics of CK-MB patients **in Group A**

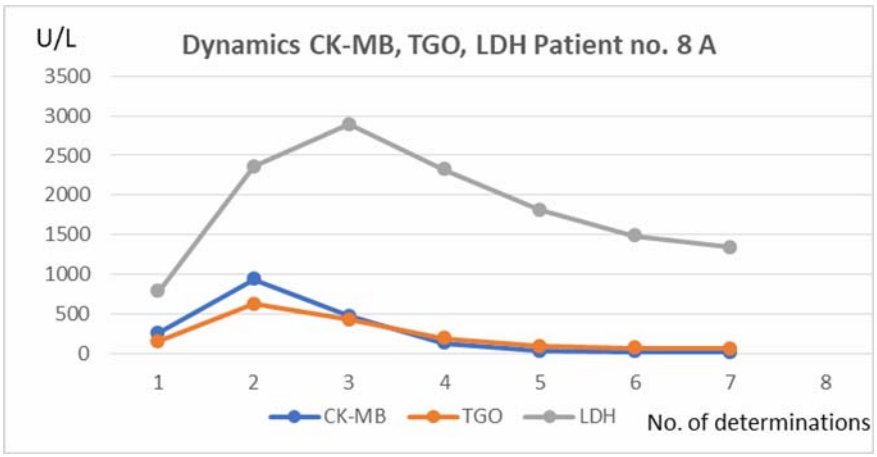

Fig. 8. Dynamics CK-MB, TGO, LDH, patient no. 8A

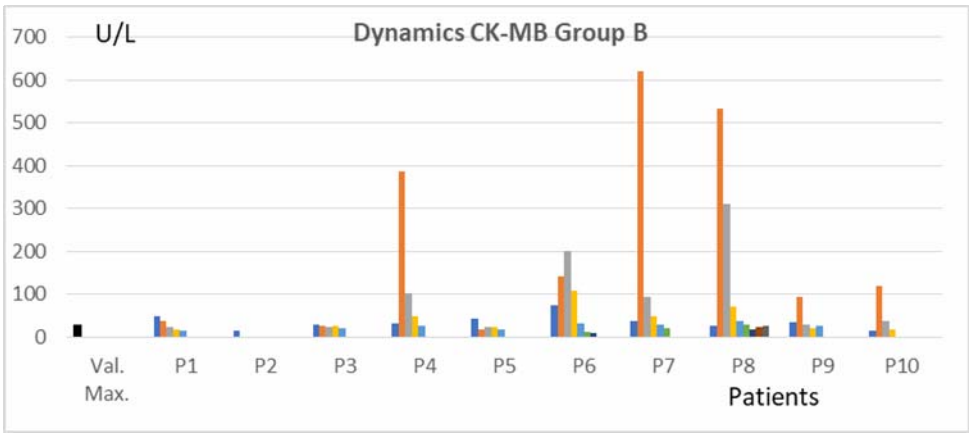

Fig. 9. Dynamics of CK-MB patients **in Group B**

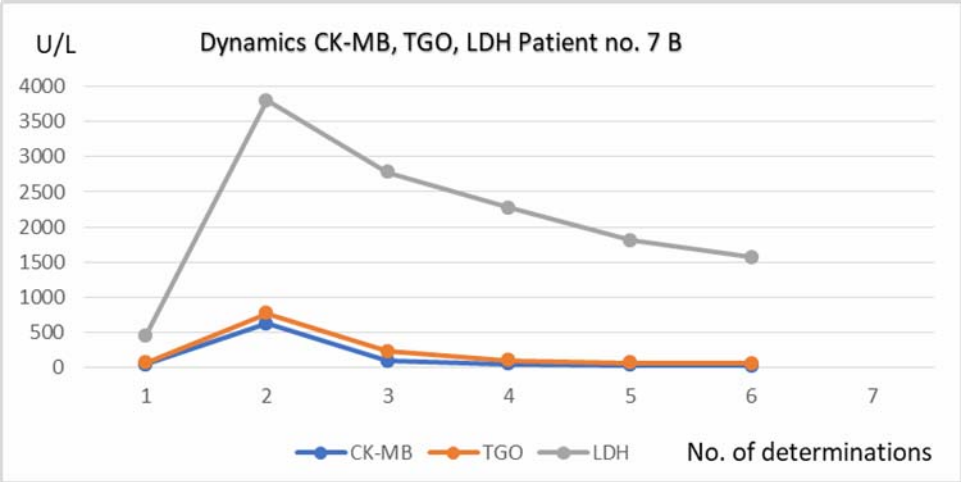

Fig. 10. Dynamics CK-MB, TGO, LDH patient no. 7B

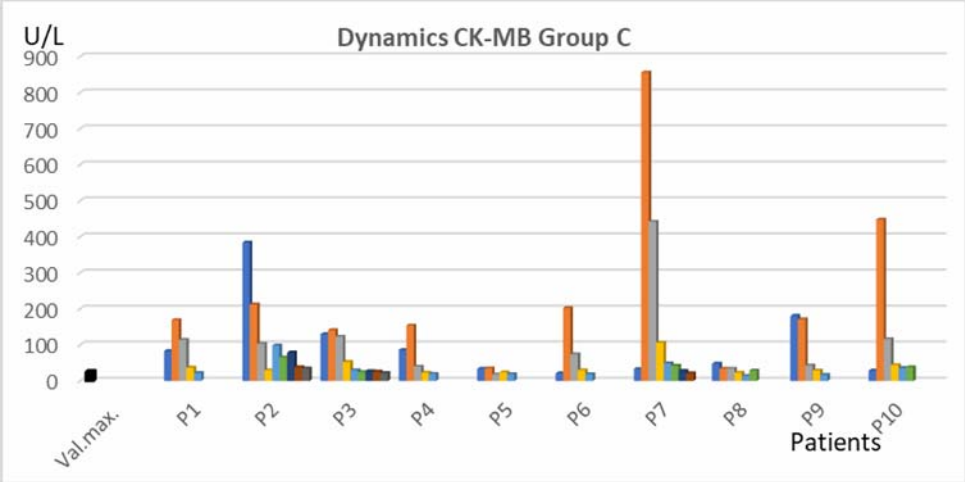

Fig. 11. Dynamics CK-MB **group C**

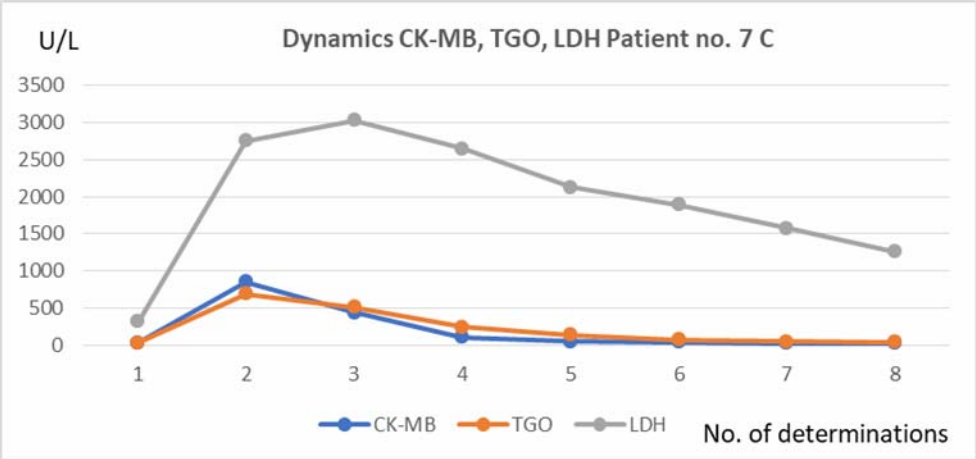

Fig. 12. Dynamics CK-MB, TGO, LDH patient no.7C

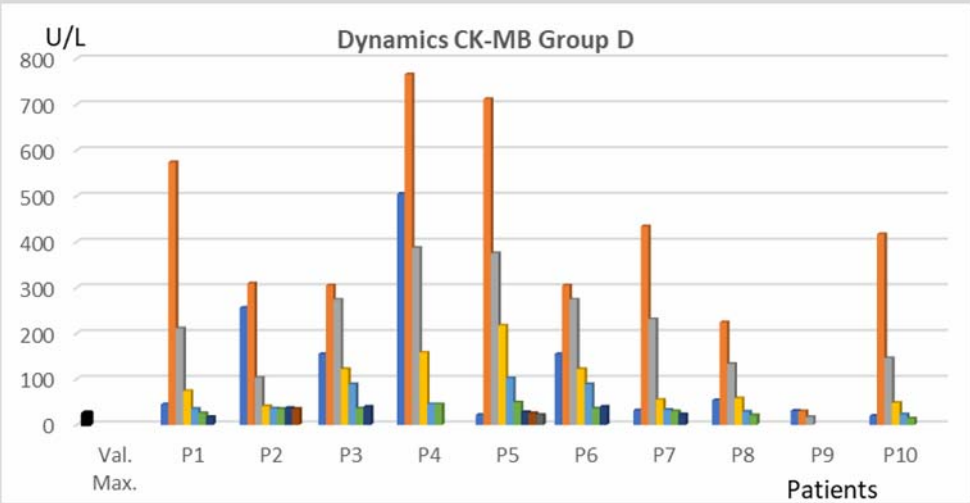

Fig. 13. Dynamics CK-MB **group D**

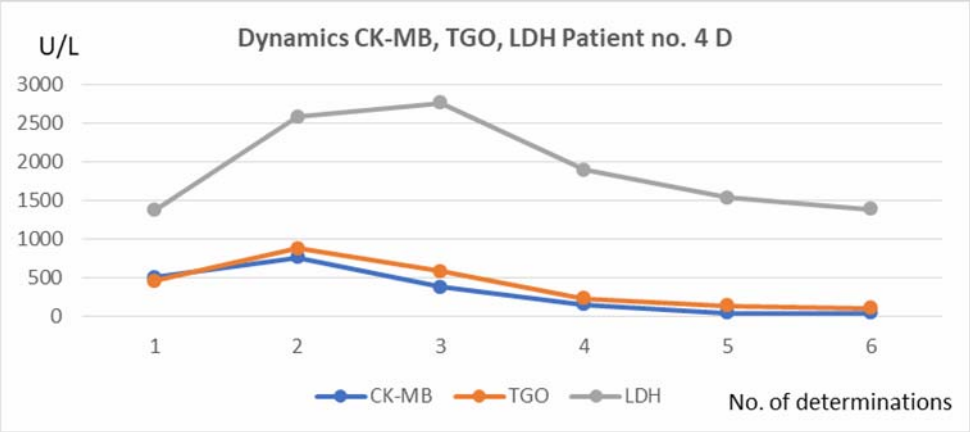

Fig. 14. Dynamics CK-MB, TGO, LDH patient no. 4D

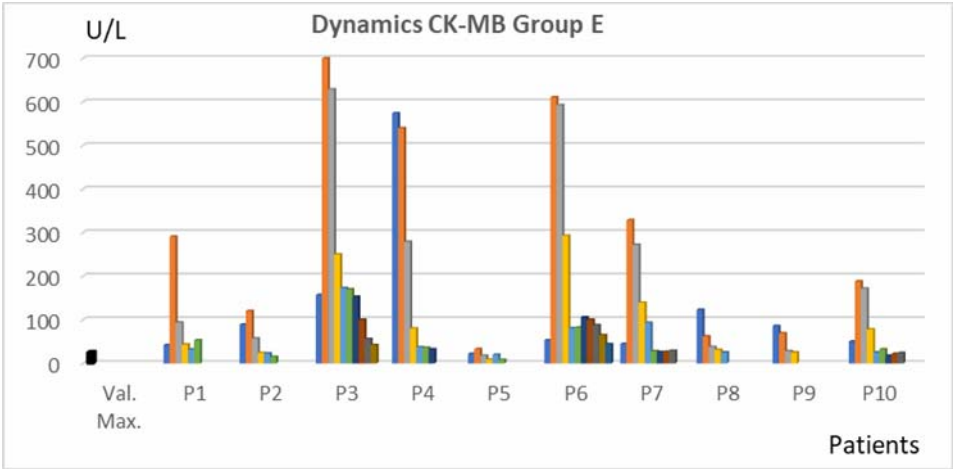

Fig. 15. Dynamics CK-MB in patients with IMA **group E**

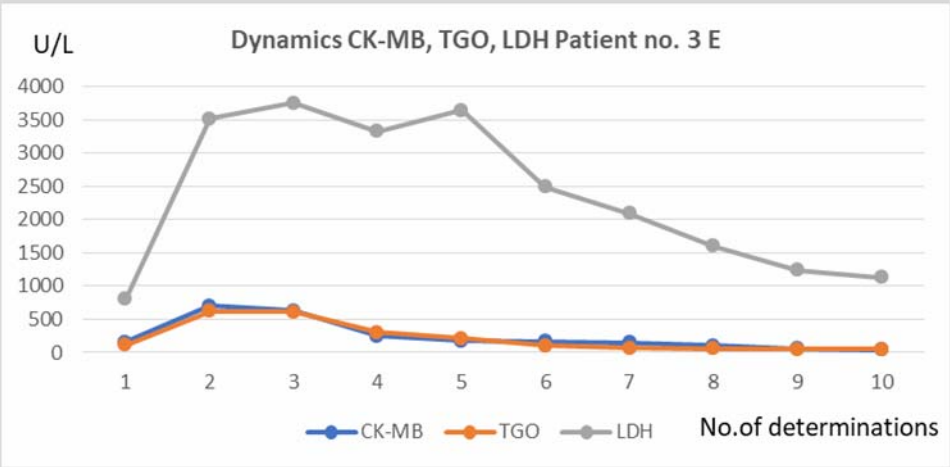

Fig. 16. Dynamics CK-MB, TGO, patient no.3E

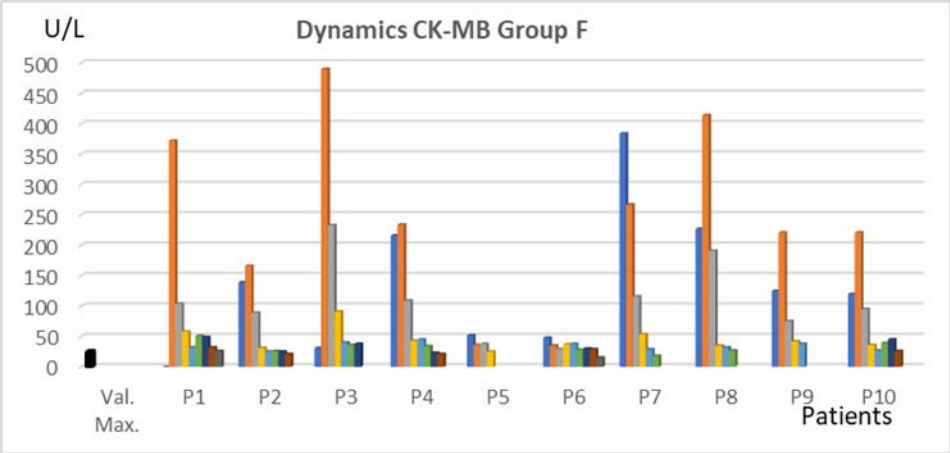

Fig. 17. Dynamics CK-MB in patients with IMA, **group F**

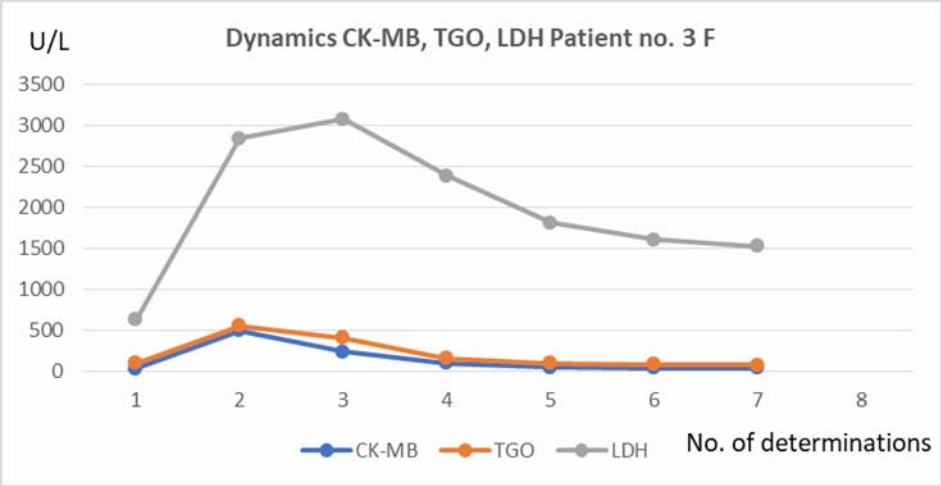

Fig. 18. Dynamics CK-MB, TGO, LDH patient no. 3F

CONCLUSIONS

- Cardiovascular emergencies occur from very young age: patients with acute myocardial infarction (AMI) of 25 and 26 years were registered.
- In young people, the immutable risk factors (sex, heredity, family history) determine the onset of coronary heart disease.
- Of the 1028 patients with AMI admitted during 2016, 70% are men and 30% are women. Male sex is considered a risk factor for cardiovascular disease, as evidenced by studies conducted over decades *(Framingham Risk Score and SCORE Project)*.
- In the age group 30-39 years in women there is no case of AMI, instead it appears in a relatively low percentage in the age group 40-49 years. The low incidence of AMI in young patients is due to estrogen hormones, which play a role in endothelial protection. Estrogens promote vasodilation and improve lipid profile.
- The incidence of coronary heart disease at very young age is low, but it increases progressively with age due to the accumulation of modifiable risk factors (diabetes, high blood pressure, dyslipidemia, obesity, smoking, sedentary lifestyle) and the atherosclerosis process which increases proportionally with aging.
- Of the 62 patients diagnosed with AMI, 35% were admitted in the winter months, with the highest number of hospitalizations (19.5%) in January. Vasoconstriction at the coronary level due to the low temperatures, being one of the reasons, as well as non-compliance with diet and medication regimes during the winter holidays.
- Dynamic CK-MB, TGO and LDH monitoring is recommended in all patients diagnosed with IMA, indicators are followed during the hospitalization period, each patient having between 3 and 12 determinations. Two patients showed no enzymatic changes, patient 12A who presented late for the onset of infarction and patient 2B who did not have parameter changes, but the diagnosis was confirmed coronary angiography.
- The other 60 patients showed increases in these indicators. The maximum CK-MB value was recorded by patient 8A (936 U / L, 37.4 times the normal value), and the lowest was patient A10 (28 U / L), the infarction confirmation being made electrocardiographic and coronary angiography.
- TGO has a concomitant evolution with CK-MB, the maximum enzymatic level being reached within 17-20 hours, the decrease following the same route, with slightly slower normalization in some patients.
- Some of the patients who had acute myocardial infarction had as risk factors: diabetes, dyslipidemia, hypertension, smoking and obesity.

ABSTRACT

CK-MB, TGO and LDH enzymes were monitored dynamically in patients diagnosed with IMA. The incidence of coronary heart disease in very young age is low, but it increases progressively with age due to the accumulation of modifiable risk factors (diabetes, high blood pressure, dyslipidemia, obesity, smoking, sedentary lifestyle) and the atherosclerosis process which increases proportionally with aging. In men, the increased incidence of AMI appears in the age group 60-69 years. Male sex is considered a risk factor for cardiovascular disease (70% versus 30% of women). In women, the maximum number of patients is 70-79 years old. Of the 62 patients investigated, two showed no enzymatic changes. The other 60 patients showed increases in these indicators.

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