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DIAGNOSTIC VALUE OF BIOHUMORAL MARKERS OF NECROSIS AND INFLAMMATION IN PATIENTS WITH RIGHT VENTRICULAR MYOCARDIAL INFARCTION

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A b s t r a c t: *Introduction/Aim*. Patients with right ventricular myocardial infarction (RVMI) and patients with left ventricular myocardial infarction (LVMI) of the anterior wall with ST-elevation (STEMI), due to the profundity and volume of the necrosis, tend to have a more severe and more complicated clinical outcome as well as a higher mortality level compared to patients with myocardial infarction of inferoposterior localization in the left ventricle (IPILK), without the right ventricle being overtaken.

C-Reactive protein (CRP) is a sensitive and reliable indicator of acute inflammation and is in good correlation with creatin kinasis (CK) or the enzymes which indicate necrosis markers in acute myocardial infarction (AIM). Because of this, a common biohumoral answer is of greater importance and more reliable both diagnostically and prognostically; it signifies a more severe and more complicated clinical outcome, especially on the rupture of the myocardium.

The main goal of this study was to compare the maximum values of enzymes and CRP in patients with RVMI and LVMI who had first STEMI and who were in the acute phase treated with percutaneous transluminal coronary angioplasty (PTCA).

Methods. During a six-year period (2000–05), in the Clinic for Urgent Internal Medicine at the Military Medical Academy, a total of 74 patients included in a prospective study were divided into two groups. The first group consisted of patients with RMI

19 (25.67%), and the second group of patients with LMI 55 (74.33%). The patients in both groups received a percutaneous coronary intervention (PCI), if they had been admitted in the first 4 hrs from the beginning of the chest pain, and if there were no contraindications. All the others received thrombolitic therapy, and a "rescue" PCI if needed, in the next 24–48 hours. The risk factors, clinical outcome, necrosis and inflammation biomarkers (enzymes and CRP), coronary status, restenosis of stent, and intrahospital mortality rate in the first month, as well as a long term prognosis over a period of one year, were analysed.

Results. The average age of the patients in the group with RVMI 19 (7 m + 12 f) was 66.1 $\pm$ 11y, and in the group with LVMI 55 (45 m + 10 f) 59.6 $\pm$ 13y, with a statistical trend which indicated that the patients with RVMI were older (66.1 $\pm$ 11y vs. 59.6 $\pm$ 13y, $p < 0.061$) and that women dominated (63.1% vs. 18.8%, $p < 0.001$). No statistical differences were found between the two groups of patients concerning the length and the appearance of the chest pain before admission to the hospital and the beginning of the PCI treatment, as well as risk factors such as smoking, cholesterol or diabetes. Of the total of 74 patients with the first STEMI as a primary manifestation of a coronary disease, we performed a primary PCI on 58 (78.37%), and a "rescue" PCI on 16 (21.63%) after the thrombolitic therapy during the 24–48h after admission. We had no cases of death either during the primary or the delayed PCI, or in the next 24h following the intervention.

During the hospital phase of treatment, in the group with RMI the causes of death were the rupture of the free wall of the right ventricle (1), acute pancreatitis (1), ARDS and hypostatic pneumonia (1), cerebrovascular insult (1). During the following year, one more patient died due to reinfarction of the anterior localization.

In the group with LMI, during the hospital phase of treatment 5 (9.09%) patients died: reinfarction (2), rupture of the left ventricle (1), respiratory insufficiency and severe hypostatic pneumonia (1), cerebrovascular insult (1). During the following year, 4 more patients died, sudden death (2), ischemic dilatative cardiomyopathy (2).

The total mortality rate over a one-year period of observation in the group with LMI was 9 (16.3%), and in the group with RMI 5 (26.3%).

Radionuclide ventriculography (RNV) was performed in the acute phase of myocardial infarction from 7–14 days after PCI and after 6 months in both groups as an independent indicator of the ejection fraction (EF) of both ventricles. The given results show that a statistically proven significant difference exists in the recovery of the right ventricle in acute phase RMI (49.1 $\pm$ 7.9 vs. 35.4 $\pm$ 10, $p < 0.001$), as well as after 6 months (49.2 $\pm$ 9.7 vs. 38.3 $\pm$ 11.2, $p < 0.010$) in patients with RMI.

Conclusion. Primary PCI should be done whenever it is possible with all patients who have a great volume and depth of necrosis, especially if that is the first manifestation of a coronary disease and the first acute STEMI, as were all of our patients in both groups. Our results show that older patients with RMI, and dominantly women, have a more severe and more complicated clinical outcome in the acute phase of RMI compared to patients with LMI of the anterior wall. In the longer prognosis of this case, they have a quicker and a more complete recovery of the right ventricle due to

which they have a better immediate and long term prognosis, but demand careful overseeing and energetic treatment in the acute phase of the myocardial infarction, especially considering that their treatment is often specific compared to patients with an infarction of the left ventricle.

Key words: Infarction of the right ventricle, infarction of the left ventricle, CRP, fibrinogen, the factors of inflammation, enzymes, percutaneous coronary intervention, balloon dilatation, intracoronary stent.

Introduction

Right ventricular myocardial infarction (RVMI) is an acute necrosis of a part of a heart muscle of the right ventricle which can overtake the whole thickness of the myocardium or just some of its partial layers.

Necrosis can overtake the right ventricle alone, in which case it is an isolated myocardial infarction of the right ventricle, or simultaneously take over the left and the right ventricles, in which case it is an "associated or combined" myocardial infarction (RV and LVMI) [1, 2].

Therefore, there is severe damage to the heart muscle and all of the most important structures of the heart, septum, transitory systems, inferior wall of the right ventricle and inferoposterior wall of the left ventricle, due to which clinical sympthomathology is complex, with a high mortality of 20–50%. The incidence is 13–56%, which practically means that every third patient with an inferior infarction of the left ventricle also has an associated infarction of the right ventricle (RV and LVMI) [3].

In regard to localization, RMI can be anterior or inferoposterior, and regarding the depth of the necrosis it can be a transmural (STEMI) or non q (NSTEMI) myocardial infarction. It has a specific clinical state, course, complications, treatment, prognosis and outcome [4].

RMI diagnosis is determined based on clinical state, standard and additional EKG tracing (V_1R – V_6R), echocardiography, haemodynamic criteria, biohumoral necrosis and inflammation marker response (enzymes, Se, fibrinogen, CRP). Iin the acute phase of the myocardial infarction, all of these biohumoral markers determine the level of inflammation and extent of the necrosis, but besides the diagnostic, they also have a prognostic significance, especially when a rupture of the heart is in question [5].

The Aim of the study

This was to compare the maximum values of CRP and fibrinogen as a marker of inflammation, and the enzymes CK-MB and LDH as the most signifi-

cant markers of necrosis in patients with first STEMI RMI and LVI of the anterior wall, who had been treated with PCI, for the evaluation of the clinical outcome in the acute phase of the treatment, early intra-hospital mortality, within the first month, and a long term prognosis in the following year.

Materials and Methods

Over a period of six years (2000–05) at the Clinic for Urgent Internal Medicine, at the Military Medical Academy, a prospective study included 74 patients with first STEMI who were treated with PCI and who, in terms of to the localization of the infarction, were divided into two groups. The first group was formed of patients with RMI 19 (25.67%), and the second group contained patients with LVI 55 (74.33%). 7 men (36.8%) and 12 women (63.2%) had RMI, average age 66.1 $\pm$ 11y, and 45 men (81.8%) and 10 women (18.2%), average age 59.6 $\pm$ 13y, had LVI of the anterior wall. The diagnosis was clinically confirmed by EKG, with an additional right sided lead from V_1R-V_6R, by enzyme, laboratory, coronarography, radioisotopic methods and, with the deceased, by autopsy. The patients from both groups, if admitted in the first 4 hours from the onset of the chest pain and if there were no complications, received a PCI. All of the others received thrombolic therapy and, if needed, a "rescue" PCI was performed in the next 24–48 hours. The study does not include patients who were admitted 4 hours after the onset of chest pain, nor patients with a repeated STEMI, nor does it include patients with NSTEMI or patients who had left or right bundle branch block and where the localization of the infarction could not be confirmed with assurance, nor patients who had some contraindication for PCI or the thrombolitic therapy.

CK, CK-MB, LDH and the other following enzymes were followed up every 8 hours for the first three days, CRP in the first 24–48 hours and fibrinogen in the first 48–72 hours from the beginning of hospitalization. The serum concentration CK was determined by a standard method on a Hitachi 911 Automatic Analyzer machine, with referent values 0–190 U/L. The serum concentration CRP was determined by the agglutinative method with mononuclear antibodies with CRP, on the Behring Nephelometar 100 Analyzer machine, with referent values from 0–5mg/L. Fibrinogen was determined on a Behring Nephelometar Analyzer II machine, referent values 1.8–3.5g/L. Coronarography was performed on a ADVANTAX LC General Electric Medical System machine, and the catheters used were "Cordis" – Cordis Company, N.V. Netherlands and 8–10ccm of contrast Urografin 76. Thrombolitic therapy was given by the accelerated protocol for t-PA (Actilysa-Boering Ingelheim 50mg), 15mg. bolus iv, 50mg in a 30 minute iv infusion and 35mg in a 60 minute iv infusion, with continuance of the therapy with heparin, nitroglycerin infusions, aspirin,

ACE inhibitors, beta blockers, etc. The "rescue" PCI was performed in the first 24–48 hours with all of those patients who had repeated or persistent angina or a repeated reelevation of the ST segment, after receiving the thrombolitic therapy, and whose clinical condition worsened either in the sense of developing a heart insufficiency or a threat of cardiogenic shock.

Radionuclide ventriculography (RNV) was performed after 7–14 days from admittance to the hospital for an early evaluation of the patients' condition and as an independent indicator of ejection fraction (EF) of both ventricles in both our patient groups. RNV was performed in vivo with "marked" erythrocytes with technetium 99m (^{99m} Te) in a 740MBq dosage in a Gaiting-Planar study on an "Orbiter" Siemens gamma camera. By statistical processing of all the parametrical attributes arithmetical core and standard deviations ($x \pm sd$) were calculated with the use of a Student t-test, the frequency for non-parametrical attributes was determined, and the differences were determined by a hi-square test. (κ^2).

Results

Nineteen patients had IRV, average age 66.1 $\pm$ 11y. Primary PCI was performed in 15 (78.9%) patients, and rescue PCI was performed after thrombolytic therapy in 4 (21.1%) patients. The time from the onset of the pain until hospital admission was less than four hours in 10:9 (52.6% vs. 47.4%) patients. Of all risk factors, smoking was present in 11 : 8 (57.8% vs. 42.2%), hypertension in 12 : 7 (63.1% vs. 39.9%), diabetes in 4 : 15 (21% vs. 79%), cholesterol > 5mmol/l in 15 : 4 (79% vs. 21%) patients. Disease of the 1 blood vessel was found in 11 : 8 (57,8% vs. 42,2%), stents on the culprit lesion were implanted in 13 : 6 (68.4% vs. 31.6%), and TIMI III flow was achieved in 14 : 5 (73.6% vs. 26.4%) patients. In the following first year 3 (15.78%) patients had restenosis of the stent. During the intrahospital period of treatment a total of 4 (21.05%) patients died and 1 more patient in the following year from reinfarction of the anterior localisation. A total of 5 (26.31%) patients died.

The causes of death during hospitalisation were: rupture of the free wall of the right ventricle [1], intracerebral haemorrage [1], acute pancreatitis [1], lung distress (ARDS) developed after heavy hypostatic pneumonia [1].

In the second group with anterior LMI, there were 55 (74.33%) patients, average age 59.6 $\pm$ 13y. Primary PCI was performed in 43 (78.18%), and a rescue PCI after the thrombolic therapy in 12 (21.82%) patients. 31 : 24 (56.3% vs. 43.47%) patients had a time of less than 4 hours from the onset of pain to arrival at the hospital. Among the risk factors, smoking was present in 29 : 26 (52.7% vs. 47.3%), hypertension 40 : 15 (78.2% vs. 21.8%), diabetes 11 : 44 (20% vs. 80%), cholesterol > 5mmol/l 34 : 21 (61.8% vs. 39.2%). 24 : 31 (43,6% vs. 66.4%)

Table 1 – Tabela 1

Parallel indicator of patients with RMI and LMI

Paralelni indikatori kaj pacienti so DMI i LMI

	RMI 19 5.67%)		LMI 55 0.33%		p<0.05
	yes	no	yes	no	
Smoking	11(57.89%)	8(42.21%)	29(52.7%)	26(47.3%)	0.946
Hypertension	12(63.15%)	7(36.84%)	40(78.2%)	15(21.8%)	0.485
Diabetes	4(21.06%)	15(78.94%)	11(20%)	44(80%)	0.945
Cholesterol>5mmol/l	15(78.94%)	4(21.06%)	34(61.8%)	21(39.2%)	0.262
PKI in the first 4 hours	15(78.94%)	4(21.06%)	43(78.18%)	12(21.82%)	0.378
Disease 1 coronary art.	11(57.89%)	8(42.21%)	24(43.6%)	31(66.4%)	0.562
Stent on culprit lesion	13(68.42%)	6(31.57%)	47(85.4%)	8(14.6%)	0.237
TIMI III flow after PTCA	14(73.6%)	5(26.4%)	42(76.36%)	13(23.63%)	0.819
Restenosis in first yr.	3(15.78%)	12(80%)	12(24.4%)	49(76.6%)	0.327
Total mortlity rate in the first year	5(26.31%)	14(73.69%)	9(16.36%)	46(83.64%)	0.525

had one coronary artery disease, and 47 : 8 (85.4% vs. 14.6%) a culprit lesion. TIMI III flow was accomplished in 42 : 13 (76.36% vs. 23.63%) patients. 12 (24.4%) patients had restenosis of the stent during the first year, and 3 : 52 (5.4% vs. 94.6%) patients had an intrahospital reinfaction. In the intrahospital phase of the treatment a total of 5 (9.09%) patients died due to: reinfarction of the heart [2], rupture of the left ventricle [1], respiratory insufficiency and hypostatic pneumonia [1], cerebrovascular insult [1]. During the course of following year, 4 more patients died: sudden death [2] and ischemic dilatetive cardiomiopathy [2]. The total mortality rate in a year was 9 (16.36%) patients.

Table 2 – Tabela 2

Characteristics of patients with RMI and LMI

Karakteristiki na pacienti so DMI i LMI

	DK x̄ ± sd	LK x̄ ± sd	P < 0.05
Age	66.1 ±11y	59.6 ± 13y	0.061
CKMB max	346.2 ± 175.3	372.6 ± 239.7	0.663
LDH max	1742.1 ± 689.5	1876 ± 806.5	0.553
Max. CRP 24–48h From admission	37.7 ± 41.5	61.1 ± 62.6	0.162
Fibrinogen 24–48h	4.2 ± 7.9	35.4 ± 10.0	0.380
RNV 7–14 days	49.1 ± 7.9	35.4 ± 10.0	*0.001
RNV after 6 months	49.2 ± 9.7	38.3 ± 11.2	*0.001

*sign

Discussion

The infarction of the right ventricle represents, in fact, the combined infarction of the left and right ventricles, because it affects the inferoposterior wall of the left ventricle and the inferior wall of the right ventricle; therefore it is characterized by numerous complications and with a high mortality rate. Patients with IRV have complete AV block 3–4 times more frequently, repetitive ventricle tachycardia or fibrillation 2.7 times; cardiogenic shock and mortality rate is 3–4 times more frequent in comparison to the mortality rate in patients with inferior infarction, the proof of which can be found in many studies as well as in our experience [6, 7, 8]. Due to the volume of necrosis alone and frequent complications which IRV patients suffer from, we made this comparison with the infarction of the anterior wall of the left ventricle (ILV) which had a similar clinical course and outcome [9]. Our results showed that there were no statistically proved differences between these two groups of patients concerning risk factors such as diabetes, smoking, hypertension and level of lipids. There was a statistically proved significance concerning gender, since in the group of patients with IRV females predominated (63.1% vs. 18.8%, $p < 0.001$) and there was a trend which showed that the patients with IRV belonged to the older age group (66.1 ± 11y vs. 59.6 ± 13y, $p < 0.061$) in comparison to the patients with an anterior ILV. These results could be compared with the results in other similar studies which show a worse outcome of AIM where gender and age were concerned [10]. The enzymes which, according to the standards in diagnosis AIM, were applied in the case of right ventricular infarction (RVI), and the essential intra-relation of CK and isoenzym CK-MB, were expressed as a percentage. If the CK-MB values were higher than 6% in comparison to the total CK, there was sure confirmation of the existence of necrosis in the myocardial infarction. Just for that reason we followed the maximal values CK-MB in both groups of patients. Patients who died due to cardiogenic shock, which was due to the 40% involvement of the volume of the myocardium of the left ventricle, had a significant elevation of CK-MB [11]. An early mortality rate after myocardium infarction, frequency of the pulse, extremely irregular pulse as well as the weakness of the left ventricle were also in significant correlation with the values of enzymes, which indirectly pointed out the damage to the myocardium during the acute phase of the disease [12, 13]. Elevated values of enzymes in the STEMI of inferior infarction, which were higher then expected according to EKG changes, could point to the disguised right ventricle infarction. In this way we could explain that there was almost the same mortality rate among such patients as in those with an anterior infarction where the area of the infarction was greater and evident [14]. In 17 patients with infarction of the inferoposterior wall of the left ventricle and a maximal CK value higher than 2000, the IRV was proved haemodynamically, but in contrast to this, we found that in six pa-

tients from the same group where the values were of CK were lower than 1000, none had IRV [15].

In his study, W. J. Rogers followed 35 patients; 15 patients from that group had anterior infarction, which showed that there was a good correlation between the coronarographic finding and EF fraction compared with the maximal values of CK-MB. However, this correlation was not found in 18 patients with inferior infarction in which the level of enzymes was higher than in the coronarographic finding in the damaged left ventricle. This indirectly showed the existence of the disguised IRV. We found that in 2 patients there was severe occlusion of the right coronary artery, as the typical angiographic finding for IRV [16]. If in the acute infarction of the inferoposterior localization there were significantly and unexpectedly increased values of CK or CM-MB, it meant that the EKG or other clinical findings did not show the volume of the expected necroses, we should have in mind associated IRV [14].

In our previous studies, when we compared two groups of 50 patients with IRV and inferior infarction of the left ventricle, without IRV, we proved that there was a specific enzymic model for IRV. If the values of CK exceeded the values of 1100 u/L, with following increased values of CK-MB over 120 u/L, which represented a specific enzymic model, which complete the diagnostic criteria for proving of IRV this has great importance in indicating the outcome [18]. That was certainly the logical confirmation of the fact that during the process of necrosis a much greater volume of the myocard was involved, in terms of area as well as depth, than in patients who only had inferoposterior infarction of the left ventricle [19, 20].

Maximal values of CK-MB in the group with IRV were 346.2 ± 175 u/L, which surely confirmed the diagnosis of IRV, which is in correlation with all present-day findings and studies. In the group of patients with anterior ILV the maximal values of CK-MB were 372.6 ± 239.7 U/L, which also points to the area and the seriousness of the necrosis.

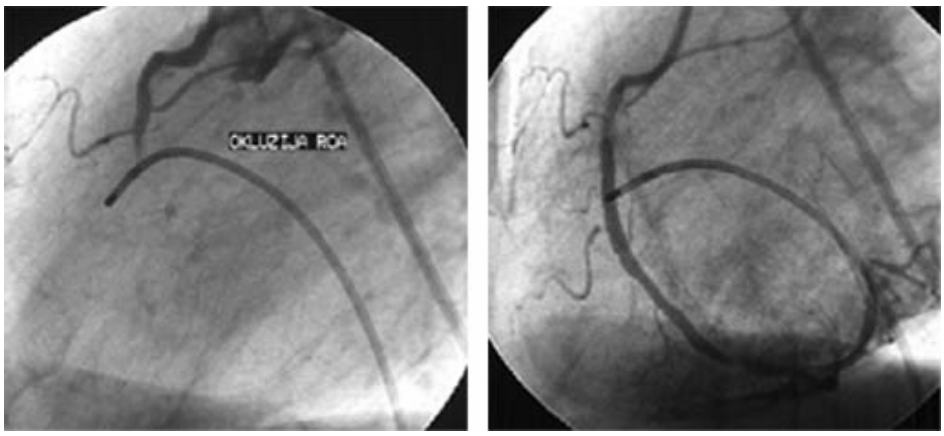
LDH values indicate the existence of a large area of necrosis, but also a higher inflammatory response, and at the same time can indicate a higher risk of myocardial rupture. In the group with RMI, LDH values were 1742.1 ± 689.5, and 1876 ± 806.5 in the group with LMI.

CRP (C-reactive protein) is a highly sensitive indicator of inflamemation, and in good correlation with CK, as a predictor of future events, especially heart ruptures, for which reason we included it in our study [21, 22]. A few of the large prospective epidemiological studies showed that a higher level of CRP in plasma indicates a reliable and independent indicator of the risk of developing a myocardial infarction, insult, peripheral vascular disease and sudden heart arrest in patients who had not been diagnosed with cardiovascular disease and were completely asymptomatic [23, 24]. CRP is one of many so-called "new risk factors" for coronary disease and a stronger indicator of the risk than

LDL cholesterol. The values of CRP increase do not change the lipid percentage and should be considered as an addition to the lipid evaluation. [25]. The additional value of CRP to the lipid screening in the form of evaluation of coronary risk was promoted within the framework of the Framingham Risk Score [26]. It was shown that the fibrinogen which was also a biomarker for inflammation and thrombosis was still questionable as an indicator of premature atherosclerosis, although there are numerous studies that point out its importance in predicting cardiovascular incidence. Other measurements of the sedimentation of white cells showed a difference to CRP, as unreliable within the framework of the clinical studies. It was proved that elevated values of CRP predict early and late mortality rates in acute coronary ischemia and add a predictable value to the heart troponin. [27]

Therefore, CRP is an independent indicator for future cardiovascular incidence and improves outcome information in lipid screening associated with other noninvasive methods. The degree of inflammation measured with the level of CRP is significantly preconditioned with the extensiveness of changes in the coronary arteries themselves and is independent in comparison to other markers for inflammation. [28]

Maximal values of CRP IRV group taken in the period of 24–48 hours after admission to hospital were 37.7 ± 41.5 mg/dl and clearly showed an elevated inflammatory response in an acute case of necrosis of the myocardium. In the second group of patients with ILK the values of CRP were 61.1 ± 62.6 mg/dl and although the absolute values were higher in the group of patients with IIRV there was no significant statistical difference between those two groups.



Ficture 1. – (M.DJ. 67y, m.) Three hours from developing RMI, the primary PCI done with stent implantation

Slika 1 ‡ tri ~asa od ravojot na DMI, PKI, napravena so implantacija na stent

The values of fibrinogen in the group of patients with IRV were 4.2 ± 1.3 g/l, whereas the values in the group of patients with ILV were 4.0 ± 0.84 g/l. Apart from the fact that these values showed an intensified inflammatory response and were used to show indirectly the existence of necrosis, there was no statistical significance between the two groups of patients. The absolute values were slightly higher in the group with IRV, which can be put down to the older age of the patients in this group.

We should bear in mind that all the patients received thrombolitic therapy and primary PCI, and "rescue" PCI was administered within the 24–48 hours; therefore all the markers of the necrosis, as well as those of inflammatory response, were less than we would have expected, because the further process of necrosis and damage of the myocardium had been stopped [29, 30[.

From the total of 74 patients from both groups 58 (78.37%), received PCI within the first 4 hours after admission and 56 (75.67%) of them achieved TIMI III flow; 16 (21.63%) were given "rescue" PCI after they had already been given thrombolitic therapy. All the patients who received primary dilatation and stent implantation had a good clinical outcome, and there were no intra-hospital mortalities. We had a death outcome, or more complicated and worse clinical outcome only in those patients from both groups who received delayed or "rescue" PCI.

RNW, as a completely independent parameter, showed a quick recovery of the right ventricle during the intra-hospital treatment phase and almost complete restitution within the first six months in the patients with IRV, as opposed to the patients with ILV. This showed that patients with IRV are a high risk group in the acute phase, with a high mortality rate, but recover more quickly than patients with ILV. Therefore it is necessary, as soon as possible, to open the infarcted artery, most often the right one, and rarely artery circumflex, whether by thrombolitic therapy or PCI, which was also proved by our findings. The volume of the right ventricle is 5–6 times smaller than the volume of the left ventricle, and therefore the need for oxygen supply is less, and the stress pressure on the wall of the right ventricle is about ten times less than the stress pressure on the wall of the left ventricle, because the pressure in the pulmonary circulation is about ten times less than in the system circulation. Besides this, the coronary flow is predominantly done in the systola with a better collateral flow in the area of the right coronary artery, so the myocites are better protected in this area in the case of the development of necrosis, and these are the factors that contribute to a more rapid recovery of the right ventricle [31, 32].

Conclusion

In conclusion we can say that our results showed that the patients with IRV were elderly patients in their age-group in comparison to the patients with

anterior ILK (66.1 ± 11y vs. 59.6 ± 13y), which predominantly affected women (63.1% vs. 36.9%) and in the acute phase these have a more severe and more complicated clinical course than patients with ILV of the anterior wall. Therefore it is essential, without any doubt, to apply reperfusion therapy whether with thrombolitic therapy or with PCI immediately after admission to hospital, because that is the only way to prevent a high mortality rate and numerous complications caused by the great volume of necrosis.

Our study shows that the modern way of treating IRV significantly decreases the mortality rate and complications in the acute stage of myocardial infarction of the right ventricle (IRV). If the opening of the infracted artery is done, rapid recovery can be achieved in the intrahospital phase and therefore a full recovery is achieved within the first six months. On the other hand, patients with anterior ILV do not have such a quick recovery in the acute phase, and therefore they do not have a better long-term outcome than patients with IRV.

The adjuvant biohumoral markers of necrosis and inflammation completely confirm not only the clinical status and diagnosis but also the predictive factors of the short term and long term outcome for such patients. This especially refers to patients with IRV, because data are scarce and rare in the available literature, which, of course, requires further follow up and investigation of this problem.

In further research into acute myocardial infarction (AMI) it is necessary, besides determining the enzymes, to follow the values of CRP because this is a valuable indicator of future cardiovascular events, especially the rupture of the myocardium, and it is a very sensitive marker of inflammation which should be in good correlation with CK-MB and troponin. This is especially very important for a better understanding of pathophysiological changes within the inflammatory response in the process of arteriosclerosis and acute coronary ischemia.

REFERENCES

1. Andersen HR., Nielsen D. (1987): The normal right chest electro-cardiogram. *Electrocardiol*; 20: 27–32.

2. Bairey N., Hah PK. (1987): Electrocardiographic differentiation of occlusion of the left circumflex versus the right coronary as cause of inferior acute myocardial infarction. *Am J Cardiol*; 60: 456.

3. Boden WE., Sadaniantz A. (1985): Ventricural septal rupture during ibuprofen therapy for pericarditis after acute myocardial infarction. *Am J Cardiol*; 55: 1631–32.

4. Adams J., Abendschein D., Jaffe A. (1993): Biochemical markers of myocardial onjury: Is MB creatine kinase the choice for the 1990s? *Circulation*; 88: 750–63.

5. Mehta S., Eikelboom J., Natarajan M. (2001): Impact of right ventricular involvement on mortality and morbidity in patients with inferior myocardial infarction. *J Am Coll Cardiol*; 37: 37–43.

6. Chockalingam A., Gnanavelu G., Subramaniam T. (2005): Right ventricular myocardial infarction: Presentation and acute outcomes. *Angiology*; 56: 371–6.

7. Lupi-Herrera E., Lasses LA., Cosio-Aranda A. (20020: Acute right ventricular infarction:clinical spectrum, results of reperfusion therapy and short-term prognosis. *Coron Art Dis*; 13: 57–64.

8. Phisterer M. (2003): Right ventricular involvement in myocardial infarction and cardiogenic shock. *N Engl J Med*; 362: 392–4.

9. Tahirkheli N., Edwards W., Nishimura R. (2000): Right ventricular infarction associated with anteroseptal myocardial infarction. A clinicopathologic study of nine cases. *Cardiovasc Pathol*; 9: 175–9.

10. Cheng C., Yeh KH., Chang HW. (2004): Comparison of baseline characteristics, clinical features, angiographic results, and early outcomes in men vs. women with acute myocardial infarction undergoing primary coronary intervention. *Chest*; 126: 47–53.

11. Norton M., Letizia M., Jennrich JA. (1993): Right ventricular infarction vs. left ventricular infarction: Rewiew of pathophysiology, medical treatment and nursing care. *Medsurg-Nurs*; 2: 3, 203–9.

12. Sobel BE., Bresnanan GF. (1972): Estimation of infarct size in man and its relation to prognosis. *Circulation*; 46: 640.

13. Strauss HD., Sobel BE. (1980): The influence of occult right ventricular infarction on enzymatically astimed infarct size, haemodynamics and prognosis. *Circulation*; 62: 3, 503–8.

14. Weinshel AJ., Isner JM. (1983): Peak CPK in transumral inferior wall infarction of the left ventricle: clue to presence or absence of coexistent right ventricular myocardial infarction. *Circulation*; 68: 391.

15. Penther Ph., Boschat J., Roudaut JY. (1983): L'infarctus isol, du ventricule droit par arth, roscl, rose, st, nosante d'une artsre coronaire droite ″courte″. Etude anatomique, clinicque et angiographique. *Arch Mal Coeur*; 76: 6, 695–702.

16. Rogers WJ., McDaniel HG. (1977): Correlation of angiographic estimates of myocardial infarct size and accumulated release of creatine kinase MB isoenzyme in man. *Circulation*; 56: 2, 199–205.

17. Lew AS., Welss AT. (1985): Precordial ST segm. Depression during acute inferior myocardial infarction: early thallium 201 scintigraphic evidence of adjacent posterolateral or inferoseptal involvement. *J Am Coll Cardiol*; 5: 203–9.

18. Orozović V. (2002): Klinička simptomatologija, neinvazivna i invazivna dijagnostika infarkta miokarda desne komore. U knjizi: Infarkt miokarda desne komore – dijagnostika i terapija. *Nauka*, Beograd; pp. 81–5.

19. Hunt PJ., Espiner EA., Nicholls MG. (1996): Differing biological effects of equimolar atrial and brain natriuretic peptide infusions in normal man. *J Clin Endocrinal Metab*; 81: 3871–6.

20. Kiu Y., Sato TO., Rourke B. (1998): Mitochondrial ATP dependent potassium channels: novel effectors of cardioprotecton. *Circulation*; 97: 2463–9.

21. Ridker PM. (2003): Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation* 2003 Jan 28; 107 (3): 363–9.

22. Mendall MA., Strachan DP., Butland BK., Ballam L., Morris .J, Sweetnam PM. *et al*. (2000): C-reactive protein: relation to total mortality, cardiovascula mortality and cardiovascular risk factors in men. *Eur Heart J*. 2000 Oct; 21 (19): 1584–90.

23. Quereshi Al., Suri MF., Guterman ln. (2001): Ineffective seconddary prevention in survivors of cardiovascular events in the US population : report from the Third National Health and Nutrition Examination Survey. *Arch Intern Med*; 161: 1621–1628.

24. Tracy RP., Lemaitre RN., Psaty BM., Ives DG., Evans RW., Cushman M. *et al*. (1997): Relationship of C-reactive protein to risk of cardiovascular disease in the elderly. Results from the Cardiovascular Health Stary and the Rural Health Promotion Project. *Arterioscler Thromb Vasc Biol*. 1997 Jun; 17 (6): 1121–11.

25. Ridker PM., Rifai N., Rose L., Buring JE., Cook NR. (2002): Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. *N Engl J Med* 2002 Nov 14; 347 (2): 1557–65.

26. Wood D., De Backer G., Feargeman O., Graham I., Mancia G., Pyarala K. (1998): Prevention of coronary disease in clinical practice.Recommendations of the Second Joint Task Force of European and other Societies on coronary prevention. *Eur Heart J*; 19: 1434–503.

27. Yarzebski J., Spencer F., Goldberg RJ., Lessard D., Gore JM. (2001): Temporal trends (1986–1997) in cholesterol level assessment and management practices in patients with acute myocardial infarction:a population-based perspective. *Arch Intern Med*; 161: 1521–1528.

28. Wilson PWF., D. Agostino RB., Levy D., Belanger AM., Silbershatz H. Kannel WB. (1998): Prediction of coronary heart disease using risk factor categories. *Circulation*; 97: 1837–1847.

29. Elsman P., van't Hof A., Hoorntje J. (2006): Effect of coronary occlusion site on angiographic and clical outcome in acute myocardial infarction patients treated with early coronary intervention. *J Am Coll Cardiol*; 97: 1137–41.

30. Vargas-Barron J., Castillo-Mora G., Lopez-Meneses M. (2002): Comparation of short and long-term benefits of reperfusion in single-vessel inferior wall acute myocardial infarction with and without right ventricular wall infarction. *Am J Cardiol*; 90: 144–7.

31. Bowers T., O'Neill W., Pica M. (2002): Patterns of coronary compromise resulting in acute right ventricular ischemic dysfunction. *Circulation*; 106: 1104–9.

32. Goldstein H. (2002): Pathophysiology and management of right heart ischemia. State-of-the-art paper. *J Am Coll Cardiol*; 40: 841–53.

Rezime

DIJAGNOSTI^KI VREDNOSTI NA BIOHUMORALNI MARKERI NA NAUROZA I VOSPALENIE KAJ PACIENTI SO INFARKT I MIOKARD NA DESNATA KOMORA

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Voved/Цел: Акутниот инфаркт на миокард на десната комора (ИМДК) и инфаркт на миокард на левата комора (ИМЛК) на преден sид со СТ елевација (СТЕМИ) заради длабочина и пространство на некроза имаат потежок и компликуван клинички тек, како и поголема смртност во однос на инфаркт од инферопостериорна локализација на левата комора (ИПИЛК) без зафаќање на десната комора.

(ЦRP)-реактивниот протеин е сензитивен и сигурен показател на акутна инфламација и е во добра корелација со креатин киназа (ЦК) и останатите ензими, кои претставуваат маркери на некроза кај акутниот инфаркт на миокардот (АИМ). Заради тоа заедничкиот биохуморален одговор има поголемо и посигурно дијагностичко и прогностичко значење, бидејќи укажува на тежина и покомлициран клинички тек, посебно на руптура на миокардот.

Цел: цел на работата беше кај болните со ИМДК и ИМЛК кои имаа прв СТЕМИ и кои во акутна фаза беа лечени со перкутана транслуминална коронарна ангиопластика (ПТЦА), да ги споредиме максималните вредности на ензимите и ЦРП-ин, кои како и биохуморалните маркери на некрозата и инфламацијата, индиректно укажуваат на длабочината и величината на некрозата во АИМ.

Методи: Во период од шест години (2000–2005 година) на Клиниката за ургентна интерна медицина на Воената медицинска академија (ВМА) со проспективна студија беа опфатени вкупно 74 болни, кои беа поделени во две групи. Прва група е со 19 болни со ИДК (25,67%) и втора група со 55 болни со ИЛК (74,33%). Заболените од двете групи веднаш по приемот во Клиниката добиле тромболитичка терапија, или биле третирани со перкутана коронарна интервенција во тек на идните 24–48 часови. Беа анализирани факторите на ризик, клиничкиот тек, биомаркерите на некроза и инфламација (ензими и ЦРП), коронарниот статус, рестенозата во стентот и интрахоспиталниот морталитет во првиот месец, како и долгорочната прогноза во текот на годината.

Резултати: Просечната старост во групата со ИДК (7 м + 12 ж) е 66,1 ± 11 г, а во групата со ИЛК (45 м + 10 ж) 59,6 ± 13 г, со статистички тренд кој покажуваше дека болните со ИДК се во постара животна возраст (66,1 ± 11 г vs. 59,6 ± 13 г, p = 0,061) и доминираат жени (63,1 % vs. 18,8%, p = 0,001). Не е докажана статистичката разлика помеѓу двете групи на болни во поглед на траење и појава на болката пред прием во Клиниката и почеток на лекување или со тромболитичка терапија или со перкутана коронарна интервенција, како нитu во поглед на факторите на ризик, како што се пушењето, зголемените вредности на липидите во крвта, дијабетес. Од вкупно 74 болни со првиот СТЕМИ, како прва манифестација на коронарно заболување, примарната ПКА беше спроведена кај 58 (78,37%), а „спасувачка“ ПКИ кај 16 (21,63%) болни по примена на тромболитичка терапија, во текот на 24–48 часови од приемот. Немавме нитu еден смртен случај во текот на примарната или одложена ПКИ, нитu во текот на следните 24 часа од применетите интервенции. Во интрахоспиталната фаза на лекување, кај групата со ИДК причина za смрт беше руптура на слободниот sид на десната комора (1), акутen панкреатитис (1), АРДС и хипостатска пневмонија (1), цереброваскуларен инсулт (1). Во period od година кај еден починат болен, беше забележан реинфаркт со антериорна локализација.

Во група со ИЛК во интрахоспиталниот период на лекување po~inaa 5 (9,09%) болни, од реинфаркт (2), од руптура на левата комора (1), од респираторна инсуфициенција и тешка пневмонија (1) и од цереброваскуларen инсулт (1). Во period od година po~inaa уште четири болни, причина нenadejna смрт (2) и исхемиска дилатативна кардиомиопатија (2).

Вкупниот морталитет во едногодишниot период беше во група со ИЛК 9 (16,3%), а во група со ИДК 5 (26,2%) болни.

Радионуклидна вентрикулографија беше спроведена во текot на акутната фаза кај инфарктот на миокардот од 7–14 дена по ПКИ и по 6 месеци кај двете групи болни, како независен покажувач на ејекционата фракција кај двете комори. Добиените резултати покажуваат дека постои докажана статистички сигнификантна разлика на подобрување на функцијата кај десната комора, во акутна фаза ИДК (49,1 ± 7,9 vs. 35,4 ± 10, p = 0,001), како и по 6 месеци (49,2 ± 9,7 vs. 38,3 ± 11,2, p = 0,010) кај болните со ИДК.

Заклучок. Примарната ПКИ треба да биде спроведена кога е можно тоа кај сите болни кои имаат големо пространство и длабочина на некроза, а најважно кај оние болни кај кои тоа е прва манифестација на коронарно заболување и први акутни СТЕМИ, како што беа кај сите наши болни во двете групи. Нашите резултати покажуваат дека болните со инфаркт на десната комора се постари, претежно жени, и имаат потежок и покомплициран клинички тек во акутната фаза на инфарктот во однос на болните со инфаркт на предниот sид од левата комора. Во понатамошниот тек тие имаат побрзо и подобро зале~ување на десната комора, а всушност и подобра непосредна и долгорочна прогноза. Меѓутоа бараат минуциозно sledење и енергично лечење во акутната фаза на инфарктот, затоа што

нивното лечење честопати е специфично во однос на лечењето на болните со инфаркт на левата комора.

Клучни зборови: инфаркт на десната комора, инфаркт на левата комора, ЦРП, фибриноген, ензими, фактори на инфламација, балон дилатација, перкутана коронарна интервенција, интракоронарен стент.

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Dijagnostičkoto značenje na biohumoralnite markeri na nekroza i inflamacija kaj bolnite so infarkt na miokard na desnata komora

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