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DO GROWTH HORMONE AND INSULIN-LIKE GROWTH FACTOR 1 AFFECT PROGNOSIS IN PATIENTS WITH KILLIP I AND II CLASS ACUTE MYOCARDIAL INFARCTION?

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SUMMARY – We investigated concentrations and roles of insulin-like growth factor 1 (IGF-1) and its binding protein (IGF1BP-3), growth hormone (GH), insulin, and markers of insulin resistance and inflammation in acute myocardial infarction (AMI). We aimed to assess any possible association between serum GH/IGF-1 axis following AMI and short-term survival rates. A follow up study was performed in 2010. Study group consisted of 75 patients with Killip I and II class AMI. There were 30 control subjects. Blood samples were obtained within 24 hours of admission and analyzed for the aforementioned hormones. Patients were followed-up during 6 months for new cardiac events. Median GH was higher in AMI (0.96; range 0.6-2.4) than in controls (0.26; p<0.001). IGF-1 was significantly lower in AMI (123 *vs*. 132; p<0.05), and so was the IGF-1/GH ratio (p<0.001) and IGF1BP-3. Insulin was higher in study group, but without statistical significance. However, we found significant between-group differences in other markers of insulin resistance (HbA1c, glycemia, HOMA-IR) and inflammation. Simple linear correlation showed positive correlation between GH and C-reactive protein. All patients with new cardiac events had IGF-1 below median and lower left ventricular ejection fraction. In conclusion, IGF-1 may affect outcome of AMI. GH resistance might be a result of inflammatory/immune response and therefore it could be a useful prognostic marker.

Key words: *Myocardial infarction; Acute disease; Insulin-like growth factor I; Insulin-like growth factor binding protein 3; Growth hormone; Insulin; Biomarkers; Prognosis*

Introduction

There is a complex interplay of insulin-like growth factor 1 (IGF-1), growth hormone (GH) and markers of insulin resistance and inflammation in acute myocardial infarction (AMI), thus making the story of AMI difficult to understand. Whether the GH/IGF-1 axis exerts cardioprotective effects remains controversial and the underlying mechanism(s) for such actions are unclear[1]. Basic science reports have emphasized a fundamental role of IGF-1 in regulating myocardial structure and function through its beneficial effects on cardiac myocyte survival, growth, calcium signaling and differentiation[1,2]. In short, the GH-IGF-1 axis includes the hypothalamic-pituitary axis (responsible for the production of GH), GH receptors (responsible for IGF production), IGF binding proteins (IGFBP) (responsible for IGF transport) and IGF receptors (responsible for IGF action). Growth hormone stimulates the production of IGF-1 in most tissues, including the cardiovascular system. The GH/IGF-1 axis regulates cardiac growth, stimulates myocardial contractility, and influences the vascular system.

Studies revealed conflicting results related to IGF-1 in AMI and heart failure[2-5]. The Framingham and

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Rotterdam studies, population-based assessments of cardiovascular risks, have reported that a low serum IGF-1 level was associated with heart failure[2,3]. There is an interesting question waiting for answer: does the GH/IGF-1 axis influence the outcome of AMI?

To address these issues, we investigated concentrations of IGF-1, GH, insulin, markers of insulin resistance and markers of inflammation in AMI. We aimed to assess any possible association between serum GH/IGF-1 axis following AMI and short-term survival rates.

Subjects and Methods

Subjects

A follow up clinical study was performed at the Department of Cardiology, Department of Intensive Care with Coronary Care Unit and Department of Cardiovascular Diseases, Tuzla University Clinical Center in Tuzla, during the period from January to December 2010. The study included 75 consecutive patients diagnosed with AMI (also analyzed for type and localization of AMI). Patient recruitment was based on the time of admission to the hospital. Inclusion criteria for the study group were age <80 years, AMI diagnosed by the World Health Organization criteria and blood sampling <24 h of symptom onset. Exclusion criteria were Killip class III or IV, body mass index (BMI) >30 kg/m^2, acromegaly, Cushing syndrome, severe thyroid dysfunction, chronic inflammatory diseases, pregnancy and women using estrogens, patients on glucocorticoid therapy, kidney failure (end stage) and liver dysfunction/failure.

Two patients were excluded from the study according to exclusion criteria, so the analysis was performed on 73 AMI patients. Patients with AMI were followed-up for a six-month period (short-term prognosis). Most patients with AMI enrolled in the study (60 patients) were treated with primary percutaneous intervention (PCI), followed by conventional therapy (angiotensin converting enzyme (ACE) inhibitor, beta blocker, clopidogrel, acetylsalicylic acid and lipid lowering agents), whereas 13 patients were not treated with PCI (they received only the aforementioned drugs). We analyzed mortality and readmissions due to rest angina pectoris or reinfarction (new cardiac events) during the study period and examined left ventricular ejection fraction (LVEF).

Table 1. Baseline characteristics of study and control groups

	Study group	Control group
Age (years)	58.6±11.7	59±10.2
Male/female	51/22 (69.9% /30.1%)	20/10 (66.7%/33.3%)
STEMI/NSTEMI	43/30 (58.9%/41.1%)	None
Primary percutaneous intervention (PCI)	60 (82.2%)	None
Anterior *vs.* inferior wall infarction	31/42 (42.5%/47.5%)	None
Number of diseased coronary vessels		
3-vessel disease	25 (34.2%)	None
2-vessel disease	23 (31.6%)	None
1-vessel disease	24 (32.8%)	None
Left main stenosis	1 (1.4%)	None
Hypertension	30 (41.1%)	None
Previously diagnosed diabetes	15(20.5%)	None
Chol (mmol/L)	5.85±1.16	4.87±1.4
TG (mmol/L)	2.67±1.72	1.75±1.48
Smokers	28 (38.4%)	9 (30%)

Data are shown as mean ± SD or number of patients (%); Chol = cholesterol; NSTEMI = non ST segment elevation myocardial infarction; STEMI ST = ST segment elevation myocardial infarction; TG = triglycerides

Control group consisted of 30 healthy individuals presenting to the hospital for follow up check-ups (in this group, coronary disease was excluded by medical history, stress test, ultrasound and/or coronary angiography). The study and control groups were gender- and age-matched. Baseline characteristics of AMI patients and control subjects are shown in Table 1. Five patients with previously diagnosed diabetes mellitus were on insulin therapy (biphasic insulin). Mild hypertension (grade II) was diagnosed in 40% of study group patients.

The study was approved by the local ethics committee, and all patients gave their written informed consent to participate in the study.

Methods

Blood samples were obtained and analyzed for the following hormones: growth hormone, IGF-1 and

baseline insulin at Department of Nuclear Medicine, Tuzla. Fasting concentrations of these hormones were determined in blood samples obtained within 24 h of admission (the mean pain to sampling time was 9±6 h), in the morning (6:00 a.m.) in Intensive Care Unit and were measured after freezing at -20 ˚C, centrifugation and aliquoting at Department of Nuclear Medicine in Tuzla. Growth hormone was measured with IRMA^{125} Sandwich Immunoradiometric Assay (IRMA) (DiaSorin, Stillwater, USA), using automatic gamma counter for gamma emitters; IGF-1 and IGF1BP-3 were measured with radioimmunoassay (RIA) (DiaSorin, Stillwater, USA) method using 1470 Automatic Gamma Counter (Wallac Wizard, Turku, Finland). Baseline insulin was measured using IRI^{125} Immuno-Radioactive-Insulin (IRI) (DiaSorin, Stillwater, USA) on Automatic Gamma Counter (Wallac Wizard, Turku, Finland).

Complete blood count, enzymes of myocardial necrosis (troponin I, creatine kinase, creatine kinase myocardial fraction), electrolyte concentrations, glucose, urea, creatinine, uric acid, lipid profile, glycolyzed hemoglobin (HbA1c) and liver function tests were carried out by the analytical unit of our Biochemistry Department by standard methods.

The homeostasis model of assessment-insulin resistance (HOMA-IR) was calculated using the international formula (fasting glucose mmol/L x fasting insulin mU/L/22.5) on a HOMA-IR Calculator version 2.2.

Echocardiography

The left ventricular ejection fraction (LVEF) was determined using Simpson's method (rule) on two-dimensional Vivid 3 ultrasound. As stated above, we measured LVEF in AMI at baseline and six months later, and we tried to find out if LVEF correlated with IGF-1 or GH. All AMI patients were divided into two groups: patients whose IGF-1 was below median and patients whose IGF-1 was above median. We analyzed if there was a significant difference in LVEF between these two groups. Additionally, we investigated

Table 2. Concentrations of study parameters in study vs. control group and in PCI vs. non-PCI group

	Study group	Control group	p value	PCI group	Non-PCI group	p value
IGF- 1 (ng/mL)	123 (82-159)	132 (125-166)	<0.05	125 (85-159)	121 (82-150)	ns
GH (μIU/mL)	0.96 (0.6-2.4)	0.26 (0.1-0.7)	<0.001	0.97 (0.6-2)	0.95 (0.7-2.5)	ns
IGF1/GH	89 (39-245)	507 (118-1100)	<0.001	91 (62-245)	89 (39-240)	ns
IGF1BP3 (ng/mL)	2793 (2272-3637)	3680 (2850-4513)	<0.05	2791 (2272-3500)	2795 (2400-3637)	ns
Insulin (μIU/mL)	9.5 (6.3-18)	7.1 (4.9-12.6)	ns	9.3 (6.3-16)	9.6 (6.7-18)	ns
Glucose (mmol/L)	7.5 (5.8-10)	5.2 (4.8-5.5)	<0.001	7.9 (5.5-10)	7.5 (5.8-9)	ns
HOMA -IR	4.16 (1.5-8.6)	1.76 (1.2-2.4)	<0.001	4.19 (1.5-8.0)	4.15 (1.2-8.6)	ns
HbA1c (%)	5.9 (5.5-7.6)	5.5 (5.2-5.7)	<0.05	5.7 (5.5-7)	5.9 (5-7.6)	ns
CRP (mg/L)	11.8 (3.4-34)	1.65 (1.1-2.4)	<0.001	11.6 (3.4-29)	11.9 (3-34)	ns
Fibrinogen (g/L)	4.03 (2.9-6.3)	3.15 (2.9-3.9)	<0.05	4.06 (2.9-6)	4.1 (3-6.3)	ns

Values are presented as medians with lower and upper quartiles in brackets, followed by p-value according to Mann-Whitney analysis; PCI = percutaneous coronary intervention; IGF-1 = insulin-like growth factor 1; IGF1BP3 = insulin-like growth hormone 1 binding protein 3; GH = growth hormone; HOMA-IR = index of insulin resistance; HbA1c = glycolyzed hemoglobin; CRP = C-reactive protein; ns = nonsignificant

Table 3. Values of study parameters in patients with new fatal and nonfatal cardiac events during follow up period

Fatal (No 1-No 3) and non fatal (No 4-No 8) cardiac events	Patient No 1	Patient No 2	Patient No 3	Patient No 4 Reinfarction	Patient No 5 Reinfarction	Patient No 6 Reinfarction	Patient No 7 AP	Patient No 8 AP
IGF-1 (ng/mL)	102	120	122	17.04	45.9	100	122	120
GH (μIU/mL)	0.25	9.51	0.97	1.24	1.78	1.19	1	2
IGF1/STH	408	12.6	127	14.03	25.79	84.03	123	110
IGF1BP3 (ng/mL)	4305	3296	2367	4513	2367	1324	3787	2229
insulin (μIU/mL)	22.5	66.6	8.1	2.6	5.6	17.4	2.3	6.3
Glucose (mmol/L	12.4	9.6	5	6.8	6.2	7.6	10	8.5
HOMA-IR	12.4	28.42	1.8	0.8	1.54	7.42	1.02	2.38
CRP (mg/L)	11.9	218.8	14.9	14	11.8	9.7	78.6	24.2
Fibrinogen (g/L)	8	6.56	2.69	2.8	5.7	7	6.05	5.8

AP = angina pectoris (rest angina pectoris); CRP = C-reactive protein; GH = growth hormone; HbA1c = glycolyzed hemoglobin; HOMA-IR = index of insulin resistance; IGF-1 = insulin-like growth factor 1; NSTEMI = non ST segment elevation myocardial infarction; STEMI = ST segment elevation myocardial infarction

mortality rate and the rate of readmissions due to reinfarction or rest angina pectoris during 180 days and tried to find out if IGF-1 level at admission influenced these rates.

Statistical methods

The SPSS v.15 software (SPSS Inc., Chicago, Illinois, USA), Arcus Quick Stat and Microsoft Excel XP Professional were used on statistical analysis. Variables with asymmetric distribution were summarized as medians and interquartile ranges. Normality tests (Shapiro-Wilk) were used for all variables. On comparison of AMI patients and control subjects, continuous variables that were normally distributed were analyzed with two-tailed t-test and unequally distributed variables were analyzed with Mann-Whitney U test. Categorical data and proportions were analyzed with the χ^2-test or Fisher exact test where appropriate. Regression and correlation analysis was also employed, as well as the receiver operator characteristic (ROC) analysis. A value of two-sided $p<0.05$ was considered significant.

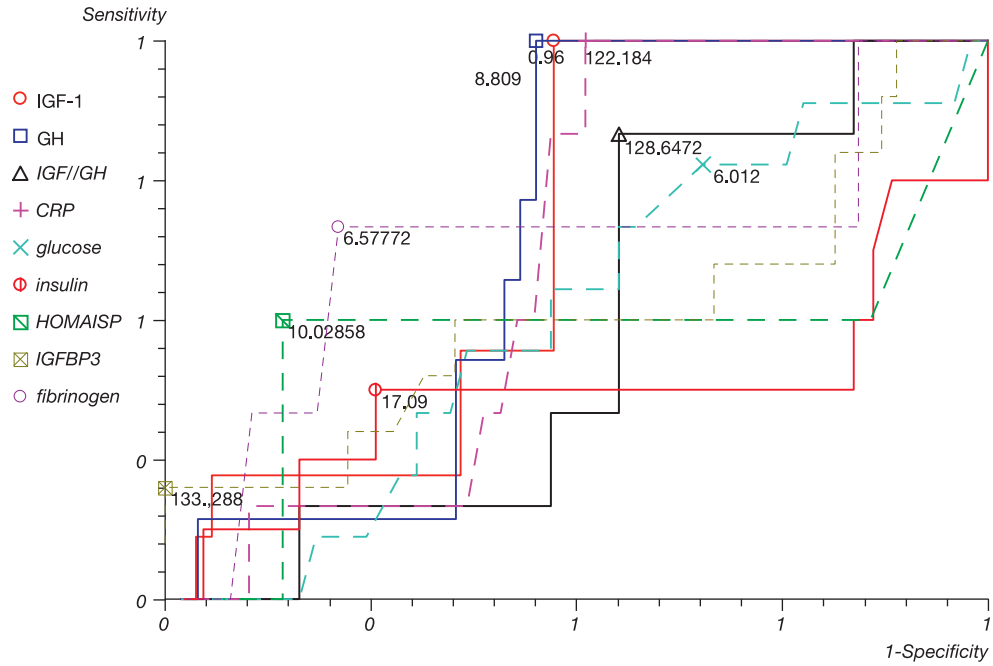
Results

The control and study groups did not differ according to age, gender and/or BMI. Shapiro Wilk test showed that variables were not normally distributed, so Mann-Whitney test was performed to analyze all study parameters except for IGF1BP-3. We found no statistically significant difference between the study group and control group only when it came to insulin, although there was a strong tendency toward it. All other parameters evaluated showed statistically significant between-group differences.

Median values with lower and upper quartile, and p values are shown in Table 2. There were no statistically significant differences in study parameters between the subgroups of AMI patients treated and not treated with PCI (Table 2).

Simple linear correlation analysis showed positive linear correlation between GH and C-reactive protein (CRP) ($r=0.350255$; $p=0.0158$) and between IGF-1 and IGF1BP-3 ($r=0.584808$; $p<0.0001$). However, there was no linear correlation between GH and LVEF or between IGF-1 and LVEF.

Age, sex, BMI, prevalence of diabetes mellitus, hyperlipidemia, hypertension, smoking, obesity and Killip classification were not different between the patients with and without new cardiac events. The subgroup of patients treated with PCI did not have better outcome as compared with non-PCI patients (in fact, all patients with new cardiac events were in the PCI group). All patients with new cardiac events (fatal and nonfatal) had IGF-1 below median (IGF-1<123, range 82 to 159). Seven of eight patients had the GH level above median and IGF-1/GH ratio below median. During follow up period, all patients with new



CRP = C-reactive protein; GH = growth hormone; HbA1c = glycolyzed hemoglobin; HOMA-IR = index of insulin resistance; IGF-1 = insulin-like growth factor 1

Fig. 1. Receiver operating characteristic curve (ROC) analysis of study parameters during follow up period.

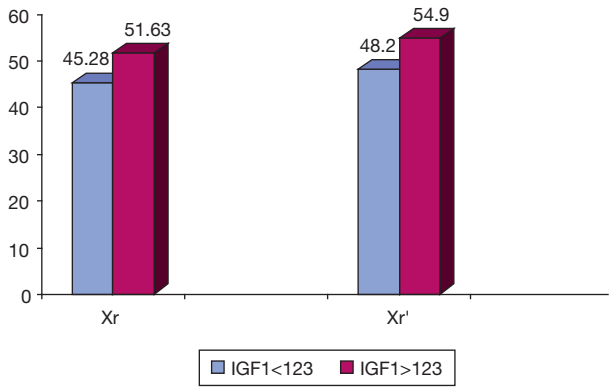
Table 4. Receiver operator characteristic (ROC) analysis of patients with and without new cardiac events during follow up period

	Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area under the curve
IGF-1	123.04	1	0.528	0.264	0.528	0.611
GH	0.96	1	0.549	0.233	0.549	0.624
IGF1/GH	128.65	0.833	0.449	0.156	0.449	0.479
IGF1BP-3	1330	0.2	1	1	1	0.507
Insulin	17.09	0.375	0.744	0.214	0.744	0.375
CRP	8.8	1	0.489	0.198	0.489	0.585
Fibrinogen	6.57	0.667	0.789	0.2	0.789	0.61
Glucose	6.01	0.77	0.347	0.179	0.347	0.505
HOMA-IR	10.02	0.5	0.857	0.333	0.857	0.357

IGF-1 = insulin-like growth factor 1; GH = growth hormone; IGF1BP-3 = insulin-like growth factor 1 binding protein 3; CRP = C-reactive protein; HOMA-IR = index of insulin resistance

cardiac events had impaired fasting glucose or diabetes mellitus according to the American Diabetes Association criteria. It should be noted that all patients with new cardiac events were treated with PCI. Table 3 shows study parameters in patients with new fatal and nonfatal cardiac events.

Figure 1 shows ROC analysis of parameters during follow up period in patients with and without new cardiac events. Table 4 shows the cut-off values of analyzed parameters with sensitivity, specificity, positive and negative predictive values, and area under the curve (AUC).(Fig. 1, Table 4). We point out that cut-



t=1.96 (p=0.028); t'=1.99 (p'=0.02)

LVEF = left ventricular ejection fraction; IGF 1 = insulin-like growth factor 1; Xr' = mean value in patients at 6 months; t = t-test value during hospitalization; t' = t-test at 6 months; Xr = mean value during initial hospitalization; Xr' = mean value in patients at 6 months

Fig. 2. LVEF values in acute myocardial infarction patients with IGF-1 below median and IGF-1 above median during hospitalization and at six-month follow up.

off values of IGF-1 and GH represent medians of IGF-1 and GH in AMI at the same time.

Figure 2 shows LVEF values in AMI patients with IGF-1 below median and IGF-1 above median during hospitalization and after six months. Patients with IGF-1 below median had a significantly lower LVEF during hospitalization and after six months too (Fig. 2).

Discussion

In this study, the values of insulin resistant state (HOMA-IR) in the first 24 hours following AMI were found to be higher in comparison with control group. The levels of fasting glucose concentration and HbA1c were also significantly higher in the AMI group than in control group. These results are similar to the results reported from some other recent studies[4-12]. A few well described mechanisms of hyperglycemia in AMI include insulin resistance, endothelial dysfunction, cortisol and cytokines. Baseline insulin levels showed no significant difference between the study and control groups, which is also consistent with some other investigations, although HOMA-IR was higher in AMI, mostly because of higher glucose level (insulin was also higher, but the difference was not statistically significant, so the final product of insulin and glucose (HOMA-IR) showed a statistically significant difference). In the aforementioned investigations, the authors also revealed insulin resistance without significant increase in baseline insulin[4,8]. During follow up period, all patients with new cardiac events had at least impaired fasting glucose.

Previous studies have documented a decrease in IGF-1 levels following MI[4-6]. However, the role of GH/IGF-1 axis remains unclear[1-4]. In the present study, the level of IGF-1 was lower and the level of GH higher in AMI patients than in controls ($p<0.05$ and $p<0.001$, respectively), and this finding is suggestive of GH resistance.

The IGF-1 might also be a good marker of patient outcome in AMI in the first six months. We believe that in the future, IGF-1 could be routinely measured as an outcome marker in 180 days, although new investigations need to be done to confirm this. As mentioned before, three patients died and five patients had nonfatal cardiac events during follow up, so the total number of patients with both fatal and nonfatal cardiac events was eight. This number is small for clear predictive values and new researches need to be done, but we analyzed these patients as the topic is too interesting and important. For example, Yamaguchi *et al.*[6] had five non-survivors during follow up period and they performed all analyses on that small sample.

As mentioned above, age, sex, BMI, prevalence of diabetes mellitus, hyperlipidemia, hypertension, smoking, obesity and Killip classification were not different between the patients with and without new cardiac events. Also, the subgroup of patients treated with PCI did not have better outcome than non-PCI group (in fact, all patients with new coronary events were in the PCI subgroup). All patients with fatal and nonfatal new cardiac events during follow up period had IGF-1 below median (<123; we pointed out above that patients with AMI were divided into two subgroups according to median). In other words, all cardiac mortality and other major new cardiac events were in the subgroup with IGF-1 below median, which is comparable to some other investigations[1,6] in which AMI patients were analyzed during a 90-day period. However, in the aforementioned study by Yamaguchi *et al.*[6], median of IGF-1 at admission was slightly higher than in our study (131 *vs.* 123 ng/mL), the authors followed-up patients over a shorter period then we did (90 *vs.* 180 days), and they did not measure and in-

vestigate the relationship of GH, IGF-1/GH and IGF1BP-3. Moreover, our analyses showed that low IGF-1 level at admission might be a good prognostic marker at 180 days and not only at 90 days. We have to point out that we performed ROC analysis which showed low IGF1 (cut-off ≤123) and high GH (cut-off ≥0.96) to have high sensitivity[1] and AUC in predicting new cardiac events (123 and 0.96 are medians of IGF-1 and GH, respectively). On the contrary, IGF1BP-3, the main binding protein of IGF1, had low sensitivity but high specificity, positive and negative predictive values[1].

The role of the above mentioned IGF1BP-3 is complex and still controversial, and there are conflicting results of IGF1BP-3 concentration in AMI. However, the actual role is not understood fully. A few authors found increased levels of IGF1BP-3 in AMI[13,14], whereas others report on decreased levels of IGF1BP-3 in AMI[15,16]. In addition, we found positive linear correlation between IGF-1 and IGF1BP-3, as expected. Several additional aspects associated with the role of IGF-1 in AMI deserve consideration. Conti *et al.*[4] tried to explain the reasons for decreased level of IGF-1 and its binding protein IGF1BP-3 in AMI. They discuss whether the level of IGF-1 is the cause of AMI or IGF-1 decreases secondarily in AMI, and they point out that IGF-1 also decreased secondarily due to immune/inflammatory response which exerted IGF-1/GH axis and due to low IGF1BP-3. According to them, IGF1BP-3 could change plasma half-life of IGF-1 (plasma half-life of IGF-1 is 10 h; when IGF-1 is in complex with IGF1BP-3 it could be 20 h). In other words, low concentration of IGF1BP-3 means low level of IGF-1. According to our results, IGF1BP-3 level is not an independent predictor of new cardiac events in six-month period and it does not affect patient outcome significantly but it is decreased in AMI and correlates with IGF-1.

All patients with new cardiac events (fatal and nonfatal) were stent treated, so the choice of therapy did not negatively interfere with the outcome of AMI. Seven of eight patients had the level of GH above median and IGF-1/GH ratio below median, so GH resistance appears to be linked to AMI outcome too. What is the possible explanation for this? The acute changes in GH concentration are supposed to be linked to the degree of the inflammatory reaction and stress provoked by the infarction. We also found strong positive linear correlation between CRP and GH, and similar results have also been reported elsewhere[6]. It is well known that inflammation plays an important role in the pathogenesis and course of acute coronary syndrome. Previous studies found elevated concentrations of nonspecific markers of inflammation (CRP, fibrinogen) in the first 24 hours of AMI[17-21]. We also found higher levels of CRP and fibrinogen in AMI. Above all, we found that all patients with new cardiac events had elevated values of CRP. CRP has also high sensitivity in predicting new cardiac events during 180-day period. We showed a strong positive correlation between inflammation and IGF-1 axis. Additionally, there was no linear correlation between IGF-1 and markers of inflammation or between GH/IGF-1 axis and markers of insulin resistance. Friberg *et al.*[5] found similar results as we did. Unlike this, Conti *et al.*[4] found decreased level of GH in AMI. We hypothesize that larger infarctions trigger a stronger inflammatory response and activate the GH/IGF-1 axis. This could explain such conflicting findings of GH levels in AMI. It therefore may be speculated that IGF-1/GH ratio (index of GH resistance) might be a useful prognostic marker in AMI (the lower the IGF1/GH ratio, the poorer is the outcome of AMI). Further investigations need to be done to confirm this hypothesis.

The group of patients with IGF-1 below median had a significantly lower LVEF during hospitalization and six months later, at follow up check-up. At follow up, LVEF was slightly better than in the first days of AMI in both groups but difference between the two groups was obvious. This finding is of importance because Scharin Täng *et al.*[22] indicated an important role of circulating IGF-1 in preserving cardiac structure and function both in physiological settings and post myocardial infarction. Unlike Lee *et al.*[7], we did not find linear correlation between IGF-1 and LVEF. Despite this, we found a relationship between IGF-1 and LVEF without doubt, indicating that IGF-1 plays an important role in preserving cardiac function post myocardial infarction.

At the end, we want to point out that recently Bourron *et al.*[23] measured IGF-1 in 1005 patients with AMI. They investigated whether IGF-1 at admission for AMI predicted death, all-cause death, recurrent AMI and stroke over a 2-year follow up. They concluded that low IGF-1 score was associated with an increased risk of all-cause death, recurrent AMI and

stroke in AMI patients. Their study was larger than ours and they followed-up patients longer than we did. But they did not measure IGF1BP-3, GH and insulinemia (as we did in our study), and therefore they could not exclude the role of GH (or IGF1 BP-3/insulin) in the higher risk of recurrent cardiovascular events observed in subjects with low IGF-1. The authors of this large study also said that these were potential limitations of their study. Our study was much smaller but we investigated precisely GH/IGF-1 axis and its link with insulinemia and inflammation.

Our study limitations were single-center design and relatively small number of patients with new cardiac events during short-term follow up period, thus precluding any definite conclusions.

Conclusions

The main findings of our study were lower IGF-1 and higher GH values in AMI as compared with control group. Besides low IGF-1/GH ratio, insulin resistance and elevated markers of inflammation were found in the first 24 hours of AMI. Strong linear positive correlation between CRP and GH might be the key of GH resistance state. Although further investigations are required, our results implicated that IGF-1 level might affect prognosis of AMI.

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Sažetak

UTJEČU LI HORMON RASTA I INZULINU SLIČAN ČIMBENIK RASTA 1 NA PROGNOZU U BOLESNIKA S AKUTNIM INFARKTOM MIOKARDA KLASE KILLIP I-II?

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Istraživali smo uloge inzulinu sličnog čimbenika rasta (IGF-1), njegovog vezujućeg proteina (IGF1BP-3), hormona rasta (*growth hormone*, GH), inzulina, biljega inzulinske rezistencije i upale u akutnom infarktu miokarda (AIM). Cilj je bio utvrditi utjecaj osovine IGF-1/GH na kratkoročnu prognozu AIM. U istraživanje provedeno tijekom 2010. godine bilo je uključeno 75 bolesnika s dijagnozom AIM (ispitna skupina) i 30 ispitanika kao kontrolna skupina. Uzorci krvi su uzimani unutar 24 h od prijma i potom analizirani na navedene hormone. Tijekom šestomjesečnog razdoblja pratili smo hoće li doći do pojave novih srčanih događaja; ultrazvučno se određivala ejekcijska frakcija (EF). Medijan GH bio je veći u skupini s AIM nego u kontrolnoj skupini (0,96 prema 0,26; p<0,001); medijan IGF-1 bio je znatno manji u ispitnoj skupini (123 prema 132; p<0,05), baš kao i omjer IGF-1/GH (p<0,001) i IGF-1BP-3. Inzulin je bio viši u ispitnoj skupini, ali razlika nije bila statistički značajna. Utvrđena je statistički značajna razlika u drugim glikemijskim parametrima (glukoza, HbA1c, HOMA IR) i nespecifičnim biljezima upale. Utvrdili smo pozitivnu linearnu korelaciju između GH i C-reaktivnog proteina. Svi bolesnici s novim koronarnim događajima imali su IGF-1 ispod medijana, te nižu EF. U zaključku, IGF-1 bi mogao utjecati na prognozu bolesnika s AIM. Rezistencija na GH je rezultat upalnog/imunog odgovora i mogla bi biti koristan prognostički biljeg.

Ključne riječi: *Srčani infarkt; Akutna bolest; Inzulinu sličan faktor rasta I; Inzulinu sličan faktor rasta, vezani protein 3; Hormon rasta; Inzulin; Biomarkeri; Prognoza*