Predictive Value of Content Adipocytokines in Patients with Myocardial Infarction Myocardium and Various Options Carbohydrate Metabolism Disorders

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Abstract: To evaluate the prognostic value of adipokines in patients with myocardial infarction (MI) and various glucose metabolism disorders.

Materials and methods. Consecutive patients aged ≤80 years and diagnosed with MI (380 patients, 63.4% males) were examined.The patients were classified into four groups: I, with normal glucose tolerance; II, with prediabetes; III and IV – with newly detected and previously diagnosed type 2 diabetes mellitus, respectively. Levels of insulin, C-peptide and cortisol during glucose tolerance test and basal levels of apolipoproteins AI, B100, leptin and adiponectin were determined in 113 patients with Q MI. Cardiovascular events were analysed for the next 2 years after MI. Logistic regression analysis was used to identify the risk factors of poor prognosis after MI.

Results. Elevated levels of leptin with decreased levels of adiponectin were observed in all MI patients independent of the degree of glucose metabolism disturbance. A linear trend of leptin level increase was observed starting from group I to group IV (Jonckheere's test: $J=2218.0$; $z=3.411$; $p=0.001$). Multiple regression analysis showed that the basal insulin level was an independent predictor of death during the 2 years after MI ($OR=0.639$; $p=0.033$). MI prior to hospitalisation ($OR=5.633$; $p=0.013$), basal hypercortisolaemia ($OR=5.435$; $p=0.016$), glycaemia ($OR=1.213$; $p=0.023$) and heart rate ($OR=1.051$; $p=0.032$) on admission were associated with the occurrence of repeated MI. Leptin levels ($OR=1.018$; $p=0.031$) and creatine kinase-MB fraction ($OR=1.009$; $p=0.018$) were risk factors of the occurrence of the combined end point of cardiovascular events.

Conclusion. An imbalance of adipokines was observed in MI patients regardless of the presence of glucose disorders.The levels of leptin, glycaemia, insulin and basal hypercortisolaemia were significantly associated with the occurrence of cardiovascular events during the late post-infarction period.

Keywords: diabetes mellitus; leptin adiponectin; myocardial infarction; prognosis.

E It has been shown that the combination of multiple cardiovascular risk factors in diabetes type 2 diabetes (DM2) more than doubles the mortality of patients with a heart attack myocardium (MI) [1]. Currently, factors that may have a negative impact are being actively studied. Prognosis in this category of patients. Changes in the concentration of leptin and adiponectin in plasma may be additional factors worsening prognosis in MI [2, 3]. It has been found that both low concentrations of adiponectin in plasma [4-6], and high [7, 8] are independent predictors of the development of MI and its complications. When studying leptin, most authors noted that higher plasma leptin concentrations have been associated with hypertension (AH), the development of coronary heart disease (CHD), MI and its complications [9–11]. However, it was also found that low leptin concentrations may adversely affect outcomes in IHD [12]. In the available literature there is no information on the determination of concentration adipocytokines in patients with MI and newly diagnosed disorders of carbohydrate metabolism and their impact for the forecast. Purpose To assess the prognostic value of

the content of adipocytokines in patients with MI and various variants of carbohydrate metabolism disorders.

Materials and methods A continuous sample of patients was examined (380 people, 63.4% men) under the age of 80, hospitalized for MI on days 1–5 (criteria WHO, 2005) to the First City Clinical Hospital Arkhangelsk. Presence of metabolic syndrome and abdominal obesity were detected according to the recommendations of the International diabetes Federation (2005). In accordance with the recommendations of the European Society cardiologists for diabetes, pre- diabetes and cardiovascular diseases (2007, revised 2013) with stabilization on the 10-14th day of hospitalization in the absence of DM 2, an oral glucose tolerance test was performed. 4 groups were distinguished: I - with normal glucose tolerance (NTG), II - with prediabetes (with impaired fasting glycemia or impaired glucose tolerance) (IGT), III and IV - with newly diagnosed DM 2 (vpDM2) and previously known and DM2. Were collected clinical and anamnestic data, p results laboratory examination, treatment, anthropometric examination was carried out (Table 1). In 113 patients (Group I - 36, II - 34, III - 17, IV - 26 patients) with Q-forming IM, selected by a continuous method and did not differ from the general sample in other respects, the insulin concentration was assessed, C-peptide and cortisol in an oral glucose tolerance test with the calculation of the HOMA-IR indices and QUICKI, determination of the concentration of apolipoproteins AI, B100 (APOLIPOPROTEIN AI; B100, SPINREACT, Spain), leptin (Leptin ELISA, DRG Diagnostics , Germany) and adiponectin (BioVendor , Czech Republic) on an empty stomach. At 14 healthy individuals (control group - GC) of both sexes in age ≥45 years with body mass index (BMI) ≤25.0 kg/ m 2 , without abdominal obesity, IHD and DM2 studied fasting leptin and adiponectin levels. The course of the hospital period of MI and the factors that determine the early prognosis has been described previously [13].

Long-term (within two years) outcomes were assessed in 274 (84.0%) people. Combined Endpoint included the presence of any of the following: cardiac death, unstable angina, MI, stroke, hospitalization for CAD or revascularization coronary arteries (CA). The study protocol was reviewed by the Committee on ethics at the Northern State Medical University 05.10.2009 All patients signed informed consent for voluntary participation in research . To quantitative signs with normal distribution are presented as the arithmetic mean and its standard deviation (SD), non-normally distributed, as median, 25th and 75th percentiles (Q25–Q75). Intergroup differences were assessed by parametric (t-test Student for independent samples) and non-parametric (Mann-Whitney U-test) tests for quantitative values and using χ^2 for nominal variables. For multiple comparisons, one-way analysis of variance was used, a test Kruskal-Wallis, χ^2 with Post Hoc paired comparisons with Bonferroni correction with a critical significance level of 0.008. Multiple logistic regression analysis was applied to determine the influence of the studied variables on the development of negative outcomes of myocardial infarction in patients with disorders of carbohydrate metabolism in the long term . Results and its discussion It was found that all patients with MI had a significantly elevated leptin concentration and a low concentration of adiponectin (adipocytokine imbalance) (Fig. 1). Although the general trend changes in the concentration of adipocytokines confirms the results of published studies [4-6, 9–11], the values of leptin concentration determined for the first time in our region were much higher than in other regions. work, which calls for further research. Phenomenon among residents of the city of Arkhangelsk. The low concentration of adiponectin in myocardial infarction is consistent with the results of work that studied the metabolism of this adipocytokine in men with coronary artery disease undergoing aortocoronary bypass surgery (CABG) in this region. Concentration *plasma* adiponectin in these patients did not exceed 4 µg/ml [14]. Patients with previously diagnosed DM 2 had significantly higher leptin concentrations compared with normoglycemic patients. observed linear trend of increasing leptin concentration from I up to group IV (Jonckheere's test : J=2218.0, z=3.411, p =0.001). Differences in leptin and adiponectin levels by gender (150.00 (48.52-179.00) ng / ml and 100.71 (56.30-150.75) ng / ml, p <0.001 and 4.23 (3.67–8.45) µg/mL and 3.83 (3.44–4.28) µg/mL, p<0.001 in women and men, respectively). Revealed positive correlations of medium strength between leptin concentration and obesity markers: BMI (rs =0.586; p <0.001), sagittal trunk diameter (rs =0.494; p<0.001), waist circumference (rs =0.481; p<0.001) and negative - with the concentration of adiponectin (rs = -482,

p<0.001). Associations of leptin with manifestations insulin resistance and carbohydrate disorders and lipid metabolism: HOMA-IR value (rs =0.386; p = 0.002), postprandial glycemia (rs = 0.348; p=0.003), basal insulin concentration (rs =0.352; p=0.001), basal concentration of C-peptide (rs =0.335; p=0.001), triglyceride content (rs =0.344;p=0.001), after calculating partial correlations with BMI control, they lost their statistical significance. After standardization by BMI, independent correlations of adiponectin with indicators of hyperinsulinemia and insulin resistance were revealed: basal concentration insulin (rs =-0.391; p =0.006), HOMA-IR index (rs = -0.371; p = 0.009) and QUICKI (rs =0.356; p=0.013). Over a two-year period, patients with type 2 diabetes more frequently developed recurrent MI (Table 1).Influence of metabolic factors for long-term prognosis in MI was assessed in groups II–IV, patients with normal carbohydrate metabolism were excluded from the analysis. At simple regression analysis revealed that that BMI and adiponectin levels were not associated with the development of cardiovascular events over two years after IM. Multiple Regression Results Adjusting for Traditional and Metabolic Risk Factors are presented in table.

2.The level of glycemia at admission 7.8 mmol / l and above, regardless of the presence of DM2 was a predictor unfavorable early prognosis and 2.29 times increased the risk of complications during the hospital period MI (p = 0.042) in the general sample of patients. When evaluating exposure to glycemia at admission in patients II-IV groups revealed its independent effect on the frequency development of MI in the long-term period (Table 2). Patients who died in the remote period MI had a significantly lower basal insulin concentration (10.05 (5.99–12.25) and 13.96 (10.69–20.60) μIU /mL, respectively, p = 0.021). Glycemic values at admission, as well as the frequency the incidence of basal hypercortisolemia was higher in patients with subsequent recurrent MI (8.10 (6.60–13.95) and 6.46 (5.39–9.38) mmol /L, p = 0.011; 57.1% and 28.1%, p=0.027). With a combined endpoint, leptin levels were significantly higher than in patients without it (157.0 (117.4–176.58) and 107.5 (73.0–159.5) ng /mL, p=0.009). Independent influence of metabolic factors long-term outcomes can be explained by the following mechanisms: hyperinsulinemia , which develops compensatory in response to insulin resistance , can have a potential protective effect against post- ischemic damage cardio myocytes , which is consistent with the modern concept of the "paradox obesity" in relation to the development of cardiovascular events [15];effects of hypercortisolemia explain the activation of sympathetic influences, as well as relationships with insulin resistance ; influence leptin may be associated with both direct potentiation of prothrombotic platelet aggregation with an increase in its concentration, and with indirect exposure to leptin through relationships with hypertension and obesity [16]. However, it should take into account the possibility indirect impacts for outcomes.

Conclusions

Manifestations of adipocytokine imbalance (an increase in the concentration of leptin against the background of a decrease in the concentration adiponectin) are characteristic of patients with IM regardless of the presence of disorders of carbohydrate metabolism.

Independent predictor value relative to the development of recurrent MI within two years of follow-up for patients with impaired carbohydrate exchange had a history of suffering before study hospitalization for MI (OR=5.633, p = 0.013), basal hypercortisolemia higher 600.0 nmol /l (OR=5.435, p=0.016), glycemia (OR=1.213, p=0.023) and heart rate contractions (OR=1.051, p=0.032) on admission. Basal insulin levels were independent predictor of death in the late post-infarction period (OR=0.639, p =0.033); level leptin (OR=1.018, p=0.031) and creatine phosphokinase MB fraction (OR=1.009, p=0.018) significantly influenced the development of the combined endpoint cardiovascular events within two years of MI in patients with disorders of carbohydrate metabolism.

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