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Metabolic Syndrome as a Risk Factor for Coronary Heart Disease (Review)

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ABSTRACT

Chronic heart failure (CHF) is a major medical and social problem. The increase in morbidity is due to both an increase in the life expectancy of the population and the influence of risk factors that contribute to the development and increase of circulatory failure. The combination of several atherogenic factors (abdominal obesity, insulin resistance, arterial hypertension, hyperglycemia, dyslipidemia)

Keywords:

Chronic heart failure

According to one of the first epidemiological studies in the Netherlands, the prevalence of MS was 17% in men and 32% in women (JM Dekker, 2005). In a PAMELA study involving 3200 individuals aged 25-72, the syndrome was detected in 17.6 % of men and 14.8% of women (G.Mancia et al., 2007). In Finland, when studying the young population, the average incidence of MS ranged from 9.8% - 14.3% and increased with age, amounting to 4.0 % in 24 year old patients and 25.2% in 39 year old patients (N. Mattsson, T. Ronnema, M. Juonala, JS Viikari, OT Raitakari, 2007). In general, it should be noted that in most European countries the prevalence of the syndrome is consistent with world average. The largest epidemiological studies on the prevalence of metabolic syndrome have been conducted in the United States of America. So, as a result of the NHANES study, conducted over 10 years with the participation of more than 8500 people, MS was registered in 23.7% of the adult population. In women, it occurs with a frequency of 23.4%, in men 24% (E.S. Ford, W.H. Giles, W.H. Dietz, 2002). Similar data were obtained in the ARIC study, which included

about 15,500 subjects aged 45 to 64 years. MS was diagnosed in 24% of women and 23% of men (A.M. McNeill et al., 2005). In most Asian countries, the prevalence of the syndrome is higher than in Europe. For example, researchers in India note that metabolic syndrome occurs from 22.1% to 41% of the population, depending on the region (DS Prasad, Z. Kabir, AK Dash, BC Das, 2012). According to other Indian authors, MS occurs in 26.5% of men and 31.2% of women (S. Pemminati, A. Prabha, R. Pathak, MR Pai, 2010). In China, however, there is a fairly low prevalence of metabolic syndrome. In Beijing, only 10% of the population suffers from MS, and in people older than 50 this indicator is about 20% (R.G. Sy, 2006). Of particular interest is the prevalence of the syndrome in Russia (O.Sidorenkov, O. Nilssen, A. M. Grijbovski, 2010). One of the first major epidemiological studies that reflect the picture of morbidity is a population-based study of the population of the city of Cheboksary to identify MS in a random sample. As a result, the main signs of the metabolic syndrome were identified in 20.6% of the population (M.Mamedov, N. Suslonova, I. Lisenkova et al., 2007). Another study was

conducted in Novosibirsk as part of the international project "Determinants of Cardiovascular Disease in Eastern Europe". In a multicenter cohort study in a sample of more than 10,000 people, the following data were obtained: 26% of residents aged 45-69 have MS, metabolic syndrome occurs in men in 18% of cases, and in women in 33% (Simonova G.I., 2006). In addition to socioeconomic factors, the age of the studied patients has a significant effect on the frequency of the syndrome. With age, the likelihood of developing this disease increases. Thus, according to American researchers, among people aged 20-29 years, MS occurs with a frequency of 6.7%, among 60-69 year olds 43.5%, and at the age of 70 years and over, 42.0% (ESFord, WH Giles, WH Dietz, 2002). In the PAMELA study mentioned earlier, the prevalence of MS in people 65-74 years old was 5 times higher than in people 25-34 years old (G.Manciaetal., 2007). Analysis of the gender characteristics of the spread of MS is ambiguous. Among patients with metabolic syndrome, there is evidence of a predominance of persons of both female and male gender. Some authors believe that MS is more common in women: for example, according to Russian scientists, among women in the Russian Federation, the syndrome is 40% more common than in men. This trend is especially noticeable in the age groups of 50-59 years and 60-69 years (Mamedov M.N., 2011; Lobanova, M.V., 2008). The predominance of females is noted in a number of other epidemiological studies (Simonova G.I., 2006; S. Pemminatietal., 2010; J.M. Dekkeretal., 2007). However, a number of authors have noted a higher prevalence of metabolic syndrome in men (E.S. Fordetal., 2002; G. Manciaetal., 2007). The active attention of scientists to MS is due to its close relationship with diseases of the cardiovascular system (J. Ness, WS Aronow, C. Ahn, 2000; A. Negassaetal., 2001; S. Haffner, HB Cassells, 2003; Volkov V.S., Poselyugina, O. B., 2011; O.V. Gaidarova et al., 2006; S. Srikanth, P. Depwania, 2010; X. Ma, S. Zhu, 2013). Such a relationship is expected, since most of the components of MS independently relate to risk factors for the development of coronary heart disease (S.Tas, NAAbdella, 1994; WL Lee, AM Cheung, D. Cape, 2000; A.V. Barsukov et al.,

2011; Sharipova G. Kh. Et al. 2008; Andreev V.V., 2011; K. Kalantzi, 2008; EA Paula et al., 2013). According to the INTERHEART study, the risk of developing myocardial infarction in people with dyslipidemia is 3 times higher, 87 times, with diabetes mellitus 3.08 times, with arterial hypertension 2.48 times, and with abdominal obesity 2.22 times (A. A. Gehani, A.T. Hinai, M. Zubaid, 2014). Based on the results of the Framingham study, a risk scale for the development of complications of coronary heart disease was compiled. In this scale, the main risk factors were the level of blood pressure and cholesterol, which are components of the metabolic syndrome (M.Epstein, 1999; Kukharchuk V.V., Chazova I.E., Ratova L.G., 2008). It was also noted that excess body weight is a determinant of high cardiovascular risk: patients with obesity of various degrees compared with the general population of coronary heart disease develops 2-3 times more often (W. Castelli, K. Anderson, 1986; Yakhontov D. A., BukhtiyN V., Tsibina T. T., 2010; G. Bertoncini, F. Bertanelli, A. Leone, 1999). The presence of a metabolic syndrome in itself significantly increases the risk of developing coronary heart disease (Abdellatif A.M., Shishova T.A., 2015; Nevzorova V.A. et al., 2011). A number of authors believe that the risks in the presence of MS as a syndrome are greater total risks included in its components (Makolkin V.I., 2010; Ivashkin V.T., Drapkina O.M., Korneeva O.N., 2011). When studying the metabolic syndrome in a prospective KIHD study, it was found that the risk of developing coronary heart disease is 2.9-4.2 times higher in patients with components of MS (Ivashkin V.T., Drapkina O.M., Korneeva O.N., 2011). Separately, the presence of a relationship between MS and the early onset of coronary heart disease is shown (A.N. Zakirova et al., 2015). Thus, in a study of 393 patients under the age of 50 and 393 of the control group, a reliable relationship was revealed between the early debut of cardiovascular disease and metabolic syndrome (Mychka V. B., Chazova I. E., 2009; L. Bokeria. et al., 2006). The various components of the metabolic syndrome not only affect the incidence of IHD, but also increase the risk of each other (Doshchitsin V. L., Drapkina O. M.,

2006; PG Kopelman, L. Albon, 1997) . So the simultaneous presence of obesity, diabetes mellitus and arterial hypertension worsens the clinical picture of each of the diseases and increases the risk of their development, adversely affecting the risks of developing coronary heart disease (Simonenko V. B., Medvedev I. N., Tolmachev V. V., 2011; Balzhinimaeva S. B., Tsyrenzhapova A. N., Rabdanova D. D., 2015; CM Povel et al., 2013; FDR Hobbs, E. Mcgregor, J. Betteridge, 2009) .In obese people, the probability of development AH is 50% higher than in individuals with normal body weight (Ostroumova O.D., Zykova A.A., 2011; Denisenko A.D., 2010; Oleynik va ND 2013; V. Persic, 2013).

According to the Framingham study, in men, systolic blood pressure rises by an average of 4.4 mmHg, in women by 4.2 mmHg. for every 4.5 kg above the norm. Also, obesity of various degrees increases the risk of developing diabetes by several times: I degree 3 times, II degree 5 times, and III degree 10 times (CL Chei, K. Yamagishi et al., 2008, PA Andreeva-Gateva et al. , 2014). Metabolic syndrome increases overall mortality and mortality from cardiovascular events. According to a 11-year PAMELA prospective study, people with MS have a 2–3 times higher risk of cardiovascular and overall mortality compared to people without metabolic disorders (G. Mancina, M. Bombelli, 2007). A prospective KIH D study showed that in patients with MS, mortality from coronary heart disease is 2.6–3.0 times higher, and mortality from other causes is 1.9–2.1 times higher depending on gender (HM Lakkaetal., 2002; Statkevich T.V. et al., 2010). Japanese doctors during a prospective examination of 2613 patients showed that the presence of metabolic syndrome increases the incidence of ischemic oh heart disease 2.1 times (C. L. Chei, K. Yamagishietal., 2008). In addition to affecting the frequency of coronary heart disease in general, metabolic syndrome and its individual components affect the frequency of acute coronary syndrome (ACS) (Gromnatsky N.I., Petrova G.D., 2007; L. Raposo et al., 2006; RB Singh et al., 2008). First of all, the level of glucose in the blood and the level of insulin resistance have a significant effect on the course

of ACS (T. Zornitzkietal., 2007; Srozhidinova N.Z., 2009; Doskina E.V., Tankhilevich B.M., 2013). According to the authors, more than 50% of patients with acute myocardial infarction are characterized by an increase in glucose levels (Mitkovskaya T.V., Statkevich T.V., 2009). An analysis of 15 studies examining the relationship between blood glucose and mortality noted a 3.9-fold increase in the relative risk of death in myocardial infarction in patients without a history of diabetes and blood sugar values greater than 6.1 mmol / L (A. Ceriello, 2005; M. Kosiborodetal., 2008; M. Anselminoet al., 2008). Moreover, according to some authors, in patients with type 2 diabetes there is an increase in the relative risk of nosocomial death by 70% in the case of glycemia of more than 10.0 mmol / l (Mitkovskaya T.V., Statkevich T.V., 2009; Lukyanchikov V.S., Zvereva I.V., 2009; V.N. Karetnikova et al., 2012; Munoz Roldan I., 2011; V. Gyberg et al., 2015). Similar data were obtained in a prospective GRACE study: the prognosis of patients with AMI without a history of type 2 diabetes, but with an acute glycemia in the acute period of more than 11.1 mmol / l, did not differ from the prognosis of patients with a diagnosis of type 2 diabetes (K.Franklinetal., 2004). Thus, metabolic syndrome increases the risk of developing acute coronary syndrome, and the degree of increase in risk directly depends on the level of insulin resistance and blood glucose level (D. Aronson et al., 2004; P. W. F. Wilson, Ja. B. Meigs, 2008). Metabolic syndrome affects the risk of complications of acute myocardial infarction: acute heart failure, ventricular fibrillation and cardiogenic shock (H.J. Buettner et al., 2007; P. J. Gheeraert et al., 2006; G. Andrikopoulosetal., 2013). Hyperglycemia and low values of high density lipoproteins have been shown to be independent predictors of the development of acute heart failure (M.Zelleretal., 2005). Other studies indicate that acute cardiac insufficiency of various classes (Kilip classification) occurs in patients with metabolic syndrome in 46.0%, and in the control group in 20% of cases, while among all components of MS it is hyperglycemia that has the greatest association with development heart failure (P.Deedwaniaetal.,

2008). In a study of 633 cases of hospitalization with AMI, it was shown that acute left ventricular failure, especially of the second and higher grades according to Killip, occurs significantly more often in patients with metabolic syndrome (M.Zelleretal., 2005). Similar dynamics are noted by Russian scientists: the risk of developing acute left ventricular failure in patients with MS, according to various studies, increases 2-3.05 times (Davydova E.V., 2008). According to several researchers, metabolic syndrome affects the level of damage markers myocardium. Studies shows that in the group with MS, the level of creatine phosphokinase (CPK) is 2.6 times higher compared to the control group (Davydova E.V., 2008).

A number of foreign studies have noted an even greater increase in creatine phosphokinase in patients with metabolic syndrome (Y.Uchida, S. Ichimiya et al., 2012; D. Kranjcec, V. Altabas, 2012; Z. Syedetal., 2011). Also, in patients with metabolic syndrome, an increase in troponin levels was noted compared with the control group (D. Milosz, L. Czupryniaketal., 2007). However, there are opposite literature data: during the study of 633 patients with AMI in patients with metabolic syndrome, the level of CPK and troponin was significantly lower, while acute left ventricular failure in these patients developed more often than in the control group (M.Zelleretal., 2005). In relation to the effect of MS on the risk of death and recurrent AMI, the data are contradictory. Most authors believe that the presence of MS increases the risk of death in patients with AMI (D.Tschoepe, P. Roesen, W. A. Scherbaum, 1999; A. M. J. Wassinketal., 2008). According to some researchers, the mortality rate in the acute period of myocardial infarction in the group of patients with MS is 2 times higher than in the control group (S. Lavietal., 2008). There are also studies according to which the presence of MS in patients with ACS increases the risk of developing sudden cardiac death, recurring myocardial infarction and recurrent myocardial ischemia by 34% compared with the control group (GG Schwartzetal., 2005; G. Ciobotaruetal., 2000 ; / Y. Liuetal., 2013). However, according to other

scientists, the metabolic syndrome does not increase the risk of death in the first year after AMI, despite an increase in hospital mortality in such patients. So, in a 1990 study of patients with AMI, patients with metabolic syndrome had higher mortality rates in the hospital period, but when mortality is taken into account for the whole year after the development of an acute coronary event, the indicators are equalized in different groups of subjects (MG Lee, MH Jeonetal. , 2010). Some 34 authors believe that MS without signs of diabetes does not increase the incidence of recurrent MI and death in patients with AMI (Yosefy C., 2003; R. Hoffmann et al., 2007; R. De Caterina et al., 2010) Along with the frequency of acute complications, the metabolic syndrome also affects the long-term prognosis of myocardial infarction (M. Lenzen et al., 2006; A. Nigam et al., 2006; C. Prosciaetal., 2013; Abdellatif A. M., Shishova T.A., 2015). It was shown that the presence of MS significantly increases the risk of death over the next three years by 29%, and cardiovascular events by 23% (P.Deedwaniaetal., 2008). In the case of the presence of diagnosed type 2 diabetes in the MS, these indicators increase to 68% and 47%, respectively (B. Mozejko-Pastewka et al., 2003; AM Svensson et al., 2005; GG Schwartz et al., 2005 ; M. Gruppetta, S. Fava, N. Calleja, 2010). Such forecasts are not confirmed by all authors (R. Hoffmann et al., 2007; G. R Iturry-Yamamoto, AC Zago et al., 2009). For example, in a study of 734 patients with coronary artery stenosis, the following data were obtained during the year after treatment: the presence of MS without diabetes did not increase the risk of cardiovascular events and death, while the presence of diabetes significantly increased the likelihood of these events (R Hoffmannetal., 2007; I. Gonzalez-Maqueda, 2007; MM Brooks et al., 2012; MC Bertoluciet al., 2014) Metabolic syndrome also affects the risk of developing chronic heart failure (CHF). Thus, in patients with MS, chronic heart failure in patients with metabolic syndrome develops earlier, compared with patients without metabolic disorders (A.C. Alba, D. H. Delgado, 2009; K. K. Gaddam, H. O. Ventura, C. J. Lavie, 2011). According to the Swedish prospective study,

which included 2314 men aged 50 years without heart failure, myocardial infarction, and heart valve lesions, the total incidence of heart failure 20 years after the start of the study was 2.3 per 1000 person years.

Moreover, among people with MS it was higher than for men without MS: 5.3 and 1.7 per 1000 person years, respectively (E. Engellsson, L. Lindetal., 2006). Another study also showed a significant deterioration in the prognosis of coronary heart disease and the development of heart failure in the presence of metabolic syndrome: the risk of heart failure increases by 46% even with a preserved ejection fraction of the left ventricle (W. Doehner, M. Rauchhaus, R. Ponikowskietal., 2005). researchers note that heart failure in patients with MS is more severe than in patients without a syndrome: according to questionnaires, such patients have a lower quality of life (Evtseva E. D., 2011). Also, patients with MS more often develop high functional classes of heart failure according to NYHA, and the middle class of heart failure is significantly higher (Bylyeva A. A., 2012). A number of domestic studies have also noted not only an increase in the class of heart failure, but also an increase in the average functional class of exertional angina and average BP in patients with metabolic syndrome (J. Wang et al., 2007; Davydova E.V., 2008). Thus, despite the active study of MS, many controversial issues remain, which requires further research in this area. According to foreign and domestic authors, patients with MS and type 2 diabetes are characterized by multiple and distal vascular lesions (M. G. Lee, M. H. Jeongetal., 2008; Shishkin A.N., Droганova A.S., 2014). A number of studies have noted an increase in the frequency of simultaneous damage to two or three vessels, as well as multiple lesions of the same vessels (A. Natalietal., 2000; Bakhshaliyev A. B., 2009; Bulashova O. V., 2003). Metabolic syndrome not only affects the number and volume of coronary artery disease, but is also a risk factor for the development of late complications during treatment. Such complications include the development of restenosis and cardiovascular events (M. Herzum et al., 2000; Ju. Mehilli et al., 2003; D. Z. Taizhanova et al., 2013). Restenosis - repeated

narrowing of the stented area of the vessel due to intimal hyperplasia. Type 2 diabetes mellitus and insulin resistance are among the two main risk factors for the development of this complication in patients with myocardial revascularization (SN Goyal, S. Bharti et al., 2012; C. Sosnowskietal., 2007). Pathogenetically, this effect is associated with an increase in proliferation smooth muscle cells with insulin directly and the activation of endothelium phosphoinositol-3 kinase, which also leads to the development of neointima (DM Breen, A. Giacca, 2011). In patients with metabolic syndrome, the incidence of restenosis ranges from 12 to 40% and depends on the level of glucose and the severity of insulin resistance, as well as the type of stent used as a treatment (G.Stone, C. Grines, D.Cox et al., 2002 ; Veselovskaya N.G., 2013). In a meta-analysis of Stone G et al. it was shown that the incidence of restenosis in patients with metabolic syndrome is 1.35 times higher among patients with coronary stenting. However, some researchers believe that the presence of MS without diabetes does not affect the likelihood of developing restenosis, and the available data are related to the inclusion of patients with diabetes mellitus in the study group (T. Przewlockietal., 2000; K. Nishio et al., 2005; JS Rana et al., 2005; M. Roffi, EJ Topol, 2004). To reduce the incidence of restenosis, especially in patients with diabetes mellitus and metabolic syndrome, drug-coated stents have been developed that, according to a meta-analysis of 38 different studies, can effectively reduce the incidence of this complication (J. Schofer, 2004; C. Stettler, S Wandel, S. Allemann, 2007; G. Longo et al., 2011). However, in a study that included 1809 patients with and without metabolic syndrome, there were no differences in the incidence of restenosis when using only drug-eluting stents (P. Canibus, E. Faloi et al., 2008). According to several authors, metabolic syndrome increases total mortality and mortality from cardiovascular diseases in stented patients (N. A. Shibeko et al., 2011). According to a meta-analysis by Xu D et al. in patients with MS and stenting of coronary arteries with stents with and without drug coverage, the risk of total

mortality is 2.17 times higher than in patients without metabolic disorders.

The risk of mortality from major adverse cardiovascular complications is 1.35 times higher in the group with MS. According to the same authors, during therapy with stents without drug coverage, the risk of general mortality is 2.25 times higher, and from cardiovascular complications 1.42 times higher. However, the risk of developing myocardial infarction in the group with and without metabolic syndrome did not statistically differ (D.Xu, Y. Guo et al., 2012). These data are similar to the results of other studies: for example, according to the Chinese scientist BinHu, in a study of the development of complications after stenting in 1224 patients for 35.4 months, a statistically significant increase in the frequency of overall mortality and mortality from cardiovascular events in SMS patients was obtained (Bin Hu, Yujie Zhou, 2011). Similar trends are noted in other studies. For example, data from other researchers showed an increase in the relative risk of developing CVS by 2.3 times in the case of using stents without special coverage during a year and a half of observations. It should be noted that not all researchers share a similar position, and there are a number of works showing that the presence of the metabolic syndrome does not affect the main CVS. Japanese scientists during a 12-month follow-up of 158 patients with and without metabolic syndrome did not receive a statistical difference in the incidence of CVD in the study groups (G. R. Iturry-Yamamoto, A. C. Zago et al., 2009). According to other scientists, the death rate is not so much due to the metabolic syndrome as the severity of insulin resistance and the level of glucose in the blood. So, in patients with type 2 diabetes, the prognosis is significantly worse compared to patients with MS, but without diabetes.

Conclusion: Women with metabolic syndrome were over 50 years old. Diabetes mellitus and obesity, as components of MS, were more common among women, while men showed a tendency to higher triglycerides and low HDL. The decompensated form of diabetes was significantly more common in men with MS. The

greatest influence on the volume of coronary lesions in men and women was exerted by diabetes mellitus, as a component of the metabolic syndrome. In patients with MS, angina of exertion of 3 FC and CHF III FC was significantly more often noted. The distant prognosis was influenced by all the components of the MS, but the largest contribution was made by the MS and its individual components, such as diabetes and hypertension. The presence of concentric hypertrophy and high SYNTAX scores also significantly worsened the long-term prognosis.

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