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Metabolic Syndromes and Different Types of Heart Rhythm Disorders

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Abstract: any disturbances of the regularity or frequency of the heart rhythm, as well as the electrical conductivity of the heart. Arrhythmias may be asymptomatic or palpitations, palpitations, or palpitations may be felt. Sometimes arrhythmias are accompanied by dizziness, fainting, pain in the heart, shortness of breath. Arrhythmias are detected during physical and instrumental diagnostics (cardiac auscultation, EKG, PPEKG, Holter monitoring, stress tests). In the treatment of various types of arrhythmias, drug therapy and heart surgery methods (RFA, electric pacemaker, installation of a cardioverter-defibrillator) are used.

Keywords: HEART, II diabetes mellitus.

XXI century, this is the century of future epidemics, because the number of patients with diseases is increasing: epidemics of chronic heart failure , arterial hypertension (AH), type II diabetes mellitus (DM), obesity, atrial fibrillation (AF). However, the number of people on our planet is limited, therefore, the likelihood that the same people can be involved in different "epidemics" is quite high. Indeed, we already know relatively much about the relationship between, for example, chronic heart failure and AF, hypertension and AF. This publication is devoted to another epidemic - metabolic syndrome (MS) [1], especially since MS is directly related to hypertension, DM, and obesity.

Is there any relationship between MS and cardiac arrhythmias? Apparently, the answer should be positive, and both regarding supraventricular and ventricular arrhythmias. For example, there are a large number of publications indicating that MS is a factor predisposing to AF, a favorable background for the implementation of risk factors for AF [2]. An example is the study of K. Umetani et al., 2008 [3]. The authors examined 592 patients without obvious structural changes in the heart. Of these, 32 (5%), MS 127 (21%) suffered from paroxysms of AF-atrial flutter. At the same time, paroxysms of AF-atrial flutter were detected in 12 (9%) patients with MS and in 20 (4%) patients without MS. Multivariate regression analysis showed that MS is a significant risk factor for paroxysmal atrial flutter, not related to left atrial size (> 44 mm) or age (> 70 years). Of the 5 components of MS according to the well-known scale ATP - III (Adult treatment Panel - III) correlated with a high degree of reliability with the risk of paroxysms of atrial fibrillation AF, body mass index (BMI) > 25 kg/m ^{2} . Thus, according to the authors, the high risk of atrial flutter AF in MS may be based on alimentary obesity.

H. _ Watanabe et al ., 2009 [4] conducted a large study that included 28449 examined patients, including 3716 (13%) with MS on the ATP - III scale who did not initially have AF. During the follow-up period (mean 4.5 years), AF was registered in 265 people, and the risk of AF with MS was significantly higher. All components of MS contributed to this increased risk, with the exception of elevated triglycerides.

In study V. N. _ Nicolaou et al ., 2011 [5] compared the sizes of the atria in patients with and without MS, suffering from non-valvular paroxysmal AF. Of the 60 patients with at least one episode of paroxysmal AF, 26 met the criteria for ATP - III . In patients with MS, the dimensions of the left atrium were 46.2 mm, without MS - 41.6 mm. The authors conclude that MS may contribute to the onset of AF by increasing the size of the left atrium.

The work of N . Echahidi et al ., 2011 [6], in which a large team of authors evaluates risk factors for AF after coronary artery bypass grafting. The authors point out that AF is a very common complication after heart surgery, which significantly affects the prognosis. They note that previous studies have already shown that obesity is a risk factor after surgery. They conducted a retrospective analysis of the relationship between obesity and MS, on the one hand, and paroxysmal AF, on the other hand, in 5085 patients after coronary artery bypass grafting. 1468 (29%) were obese (BMI > 30 kg/m ^{2}), 2320 (46%) had MS according to ATP - III criteria . Paroxysmal AF occurred in 1374 (27%) patients. In obesity, AF paroxysms occurred significantly more often only in patients older than 50 years. However, MS in the absence of obesity also turned out to be an independent significant risk factor for the development of AF (12% vs. 6%), regardless of age.

The relationship between QT interval prolongation and the risk of life-threatening ventricular arrhythmias is well known. In a study by S. Soydinc et al ., 2009 [10] it was shown that in 50 patients with MS, in accordance with ATP - III - criteria in comparison with the control group of 33 people were significantly higher than the minimum and maximum corrected QT interval, as well as corrected QT variance .

Another tool to assess the risk of fatal ventricular arrhythmias is the analysis of heart rate variability, which reflects the state of the autonomic nervous system. As is known, it is the autonomic nervous system that plays an important role in the initiation of malignant ventricular arrhythmias [11]. The probability of their occurrence is usually associated with an increase in the tone of the sympathetic and a decrease in the tone of the parasympathetic nervous system [12]. In the work of S. K. _ Park et al ., 2009 [13], 423 elderly men were examined (Normative Aging Study), of which 32% had MS.

Thus, we have reason to believe that the presence of MS increases the risk of AF and life-threatening ventricular arrhythmias in patients. On the other hand, MS is clearly not among the diseases that are in the field of view of those cardiologists who are specifically involved in the diagnosis and treatment of cardiac arrhythmias, that is, arrhythmologists. Information about the pathogenesis of MS is directly related to the pathogenesis of arrhythmias in this disease, and the principles of MS treatment are related to the primary prevention of cardiac arrhythmias.

In April 2007, a new edition of the European guidelines for the management of patients with hypertension was published [14]. One of the innovations of this version was that in the table of risk stratification of cardiovascular complications in patients with hypertension, MS was included as a separate item: along with multiple risk factors, preclinical ones (for example, left ventricular hypertrophy, microalbuminuria, thickening of the intima-media complex or atherosclerotic plaque in the carotid artery system) by manifestations of target organ damage and diabetes, this condition, according to our European colleagues, determines a moderate additional risk of cardiovascular complications even at a normal (120-129/80-84 mm Hg) level of blood pressure (BP), high additional risk in the range from high normal BP (130-139/8589 mmHg) to II degree AH (160-179/100-109 mmHg) and very high - with III degree AH (BP more than 180/100 mm Hg). Does this mean that MS should become part of the diagnostic formula in patients with AH? Certainly not. And the point, first of all, is that so far there is no single definition of this state .

Almost all proposed definitions include high values of waist circumference (WC) as a marker of abdominal obesity, possibly associated with tissue resistance to insulin, disorders of lipid and carbohydrate metabolism, and hypertension. But, for example, the main criteria for the presence of MS, as defined by the American Association of Clinical Endocrinologists (2002), also included purine metabolism disorders, and additional criteria also list coronary artery disease, microalbuminuria, endothelial dysfunction, coagulation disorders, and polycystic ovaries. Other definitions include markers of inflammation, primarily C- reactive protein, non-alcoholic

steatohepatosis, hepatocyte dysfunction, and any manifestation of atherosclerosis that may lead to increased cardiovascular morbidity and mortality [15]. Tightening the criteria for abdominal obesity (WC in men is not 102, but 94 cm, and in women is not 88, but 80 cm) and the concept of "disordered carbohydrate metabolism" (fasting glucose level is not 6.0, but 5.6 mmol/l) in the definition of the International Federation of Diabetologists (2005) significantly expands the circle of " matured" in the presence of MS. However, there is no evidence that such a tightening is due to a further increase in cardiovascular morbidity and/or mortality within the range of the proposed changes. A more rational approach seems to be in which “threshold”, that is, increasing the negative prognostic significance, WC values are determined depending on BMI: 87 (m) / 79 (w) cm with normal body weight, 98 (m) / 92 (w)) cm - with excess, 109 (m) / 103 (l) cm with obesity of the first degree, 124 (m) / 115 (g) cm - with obesity of high degrees [16]. It is clear that data on the prevalence of MS in a particular population is extremely dependent on which definition of this syndrome was used in the study.

For example, when using the WHO criteria [17] (Table 1), the prevalence of MS among the US adult population was 25.1%, and when using the ATP criteria - III [18] - 23.3%: seemingly very close figures, but 15-20% are different groups of people. In addition, Mexicans are more likely to have MS when using the WHO criteria, and in Mexican women when using the ATP criteria. III. In Southeast Asians, insulin resistance against the background of hypertension and lipid metabolism disorders is - often detected with a less pronounced increase in WC (94-101 cm for men and 80-87 cm for women) than in Europeans.

In other words, when different definitions are used depending on ethnicity and gender, the frequency of MS can vary within 24%. But, regardless of the criteria used, the results of all studies indicate the adverse effects of "concentration" in one patient of one or another combination of cardio -metabolic risk factors. H. _ M. _ Lakka et al ., 2012 [19], applying either ATP criteria III, or WHO criteria, selected a group of 1209 middle-aged men and followed it up for eleven years; the presence of MS, established in accordance with any of the criteria used, increased the relative risk of death from cardiovascular causes by 2.5-4 times. In addition, according to the calculated data, the prevalence of MS in the population of 60-year-olds can reach 40% [20]. Not surprisingly, according to WHO experts, MS is among the ten most dangerous diseases of modern mankind [21].

In accordance with the general medical significance, the problem of MS is discussed by specialists of various profiles: there are sections devoted to MS in the European guidelines for the primary prevention of cardiovascular diseases, and in the guidelines for the management of patients with hypertension from 2007, and in a document discussing the relationship between diabetes, pre-diabetes and cardiovascular disease. Moreover, in the fall of 2007, Russian recommendations were published, completely devoted to the diagnosis and treatment of MS. This document contains another version of MS detection criteria [22].

In June 2007, within the framework of the 76th Congress of the European Society for the Study of Atherosclerosis, a satellite symposium "Metabolic Syndrome" was held. All speeches emphasized the importance of the subject of discussion, but at the same time, the thesis was repeatedly voiced that something that has at least 20 definitions cannot be a diagnosis. But even if we are not talking about a diagnostic formula, the identification of metabolic trouble factors is an alarm that requires active action.Activity concerns both examination and treatment. If one or more of the most obvious - components of MS is identified - abdominal obesity (especially in non-obese people), dyslipidemia, - carbohydrate metabolism disorders, hypertension - a targeted search for other possible manifestations of it is necessary - hyperuricemia, left ventricular hypertrophy, microalbuminuria, increased pulse wave propagation velocity - factors that not only confirm an unfavorable prognosis, but also determine the choice of therapeutic tactics in general, and preferences for groups of drugs and specific drugs, in particular.

An example is the changing attitude towards isolated office hypertension. By definition, we can talk about isolated office hypertension if the repeated detection of blood pressure figures above 140/90 mm Hg during visits to the doctor. not confirmed by the results of daily monitoring of blood pressure. It is known that in the absence of target organ damage, the prognosis in these people is

significantly better than in patients with stable hypertension, although perhaps somewhat worse than in people with perfectly normal pressure. This fact was associated with a calm attitude towards this phenomenon. However, the new version of the European guidelines for the management of patients with hypertension indicates the need to assess, in addition to target organ damage, also metabolic risk factors, since their identification entails the obligation not only to correct the patient's lifestyle and dynamic monitoring of him, but also medical correction of the identified violations.

The inclusion of MS in the criteria for stratification of the risk of cardiovascular complications in patients with AH, naturally, suggests its influence on the choice of therapeutic tactics. So, if signs of MS are detected in a person with a normal level of blood pressure, then maximum efforts should be made to correct his lifestyle. At high normal values of blood pressure, in addition to non-drug measures, the indication of antihypertensive therapy should be considered; AH I and II degree is an unconditional indication for the appointment, after the correction of lifestyle, drugs that normalize blood pressure; with AH III degree of drug recommendations may precede the development of a program of non-drug interventions.

The appearance of a patient with MS is often an illustration of the neglect of a healthy lifestyle. Meanwhile, it is in patients with signs of MS that lifestyle correction can be especially effective. The key point in the program of non-drug interventions in this patient population is weight control, since reducing body weight to normal levels significantly reduces the risk of developing diabetes. Moreover, it is known that a decrease in total body weight by 10% provides a decrease in the mass of visceral fat by about 30%. Meanwhile, it has now been proven that visceral fat is not an inert energy store, but a real endocrine organ [23], producing about 20 biologically active substances, expressing a number of receptors capable of responding to various neurohumoral signals. As a result, this "organ" is in constant metabolic interaction with other organs and systems, influencing eating behavior, carbohydrate and lipid metabolism, performing neurohumoral and immune functions. Naturally, weight control can be carried out successfully only with an integrated approach: a healthy diet plus adequate physical activity.

Given the traditionally skeptical attitude of patients to non-drug interventions, it is advisable to avoid "restrictive" dietary recommendations. First of all, we should talk about the fact that the most varied diet is useful, including the whole variety of fresh and culinary processed vegetables and fruits, whole grain breads now available, fatty sea fish and seafood, wholesome meat, cereals and pasta durum wheat products. Although, of course, it is impossible to do without explanations about the restrictions (seafood, but not shrimp; if meat, then beef, white poultry meat without skin; fats are limited, and 2/3 are vegetable; if possible, not canned food, not sausages, not black bread - too much salt). It is difficult to overestimate the role of adequate physical activity both in achieving normalization of body weight and in improving the overall prognosis of patients.

An impressive illustration of this is the results of Nurse Health Study (2013): at the same BMI, mortality in groups with moderate and high physical activity was significantly lower than in groups with low physical activity. It is clear that “natural” physical activities at work will be the most acceptable for someone (refusal to take the elevator in favor of walking up the stairs, 5-7 km walk to work and / or home, etc.), someone he will prefer classes in the gym or swimming pool. In some cases, even an integrated approach does not provide the necessary weight loss. To date, the only drug that allows you to effectively and safely affect this process from the point of view of the cardiovascular system is Xenical, a selective inhibitor of gastrointestinal lipases. According to the Russian guidelines for the diagnosis and treatment of MS, indications for drug therapy for obesity are BMI > 30 kg/m2 ^{or} a combination of BMI > 27 kg/m2 with signs of abdominal obesity, hereditary predisposition to type 2 diabetes or its presence, dyslipidemia, hypertension .

However, in the 2007 European guidelines for the management of patients with hypertension, it is emphasized that, first of all, drugs should be used that do not increase the risk of developing new cases of diabetes. This is due to the fact that an assessment of the dynamics of the spread of DM throughout the world allows us to speak of a real epidemic of this disease: if the current trend continues, then by 2010 there will be about 221 million patients with DM on Earth, and by 2030 - 360 million [25]. Since in a number of clinical studies comparing the efficacy and safety of therapy

with "old" (diuretics and beta-blockers) and "new" (angiotensin-converting enzyme inhibitors (ACE inhibitors) and ARBs) drugs, data were obtained on the rarer development of new cases of diabetes in the treatment the latter, it was concluded that hyperactivation of the renin-angiotensin-aldosterone system plays a leading role in the development of clinically significant disorders of carbohydrate metabolism.

This class of drugs has now been shown to have an antihypertensive effect comparable to other modern BP-lowering drugs and a side effect profile comparable to that of placebo. The therapeutic niche occupied by this group of drugs is rapidly expanding and currently includes chronic heart failure, myocardial infarction, diabetic nephropathy, proteinuria/microalbuminuria, left ventricular hypertrophy, AF, MS [26].

In accordance with the versatility of MS, the therapy of this condition can only be complex, - multicomponent. At different stages, different manifestations of MS may come to the fore in different people. Therefore, in the treatment of these patients, it is advisable to prescribe, first of all, therapy aimed at correcting the currently leading symptom (be it hypertension, dyslipidemia, or hyperglycemia), and within the framework of the chosen direction, the characteristics of a particular patient should be taken into account.

Considering that the combination of any level of increased blood pressure and metabolic disorders causes a high or very high risk of cardiovascular complications, and the risk of III and risk IV are absolute indications for the initial prescription of combined antihypertensive therapy, it is fundamentally important to emphasize that in almost any case of assistance to a patient with MS, we will talk about the simultaneous prescription of an ACE inhibitor / ARB + calcium channel blocker ± I - 1 -imidazoline receptor agonist ± β-blocker ± indapamide / hydrochlorothiazide (no more than 12.5 mg / day)

In the course of a population study carried out in Finland, it turned out that over the last 10 years of the 20th century, the Finns as a nation have become much more "metabolically burdened" - the number of people with overweight, lipid metabolism disorders, at the same time, blood pressure in the average was lower. This suggests that at the population level, as well as in individual individuals, various components of MS may predominate at a particular moment. Accordingly, at a particular stage, for example, not antihypertensive, but only lipid-lowering therapy may be required.

statins are currently the drugs of choice for lipid spectrum correction due to their lipid-lowering and multiple pleiotropic effects, in particular, the ability to reduce the level of the pro-inflammatory marker of atherosclerosis progression, C-reactive protein. Since lipid spectrum disorders in MS are characterized primarily by severe hypertriglyceridemia, it is reasonable to use the most widely used drug in these patients- atorvastatin, or rising strength rosuvostatin. If, despite monotherapy with medium therapeutic doses of statins, which led to the achievement of the target LDL level (less than 2.5 mmol / l), the level of triglycerides is 2 mmol / l or more, then it is recommended to increase the doses to the maximum (80 mg atorvastatin, 40 mg rosuvastatin) or use a combination of statins with ezetimibe, nicotinic acid, or fibrates [27]. True, this recommendation is not indisputable - in the document it is classified as class IIb (benefit not well established), level of evidence B (data from one randomized or multiple non- randomized trials).

The share of DM in terms of aggravating the unfavorable prognosis in patients with MS is extremely high. For example, in North American Indians who did not have DM, there was no increased risk associated with MS. In elderly Italians with diabetes, the risk ratio for complications did not differ between those with other signs of MS and those without: the increase in risk due to dyslipidemia was “redeemed” by the diabetes itself. As emphasized in the Russian guidelines for the diagnosis and treatment of MS, the results of numerous studies indicate the importance of not only DM, but also IGT, especially postprandial hyperglycemia, for cardiovascular morbidity and premature mortality. Adequate glycemic control (according to the target program "Diabetes mellitus" - fasting glucose < 5.5 mmol/l; postprandial glucose < 7.5 mmol/l) is the cornerstone of reducing cardiovascular risk in these patients.

The drug of first choice for glycemic control in MS, at least in overweight diabetic patients, is metformin. It was assumed that the above positive properties would make metformin useful already at the stage of IGT. However, in a direct comparison of the effectiveness of only non-drug measures and only the use of metformin, it turned out that in order to prevent one new case of DM, half as many patients need to be treated non-pharmacologically than with metformin. Moreover, with simultaneous compliance with non- drug recommendations and the use of metformin, the result did not improve [27].

Taking into account the negative prognostic value, it is advisable to include aspirin in the complex drug therapy of most patients with signs of MS, and even more so in the presence of DM, for the purpose of primary prevention of coronary artery disease.

Thus, although there is no reason to consider MS as a separate disease, it certainly is not a set of random risk factors, since all the manifestations currently classified as manifestations of MS are in a pathogenetic relationship with each other. The concept of MS is useful for the formation of an integrated approach to the diagnosis, prevention, effective and safe treatment of cardiovascular diseases. The choice of therapeutic tactics should be determined by the set of MS components in a particular patient.

The question of whether MS is an independent risk factor for AF or whether this risk is made up of the contributions of individual components of MS remains open. It is he who, in particular, is discussed in the editorial article of the journal " Circulation " [28] devoted to the publication of H . Watanabe et al . [4] on the relationship between MS and FP. The authors of the editorial believe that in any case, the success of the prevention and treatment of AF in MS will depend on the adequate treatment of hypertension, diabetes, obesity, obstructive sleep apnea syndrome, that is, on the primary prevention of AF. It is this approach to treatment that is reflected in the most important recent publications on arrhythmias: ACC / AHA / ESC guidelines for the diagnosis and treatment of AF. [29] and guidelines for the treatment of ventricular arrhythmias and the prevention of SCD ACC / AHA / ESC [thirty]. So, for the first time, perhaps, in the new guidelines for AF, based on the results of a number of multicenter studies (HOPE , LIFE et al.) proposed the use of ACE inhibitors and ARBs for primary prevention of AF. As for ventricular arrhythmias, the only group of drugs for which the effect on the “end points” (reducing the risk of SCD) is absolutely proven are β-blockers.

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