METABOLIC SYNDROME: RISKS IN YOUTH SPORTS

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Metabolic syndrome is one of the pre-nosological conditions that implies strain on several systems of the body and disruption of all types of metabolism. The key components of the syndrome are visceral obesity, peripheral tissue insulin resistance, arterial hypertension and non-alcoholic fatty liver disease. There is a number of diseases associated with the syndrome, which makes diagnosing its preclinical manifestations important. Overweight and obesity only continue spreading; moreover, these conditions are registered in people of increasingly younger age. Metabolic syndrome in childhood increases the risk of cardiovascular disease in adulthood. Top tier athletes are no exception. Some sports and playing roles promote body weight growth. A young athlete may have specific constitutional features, and, without proper control, motivating such athletes to grow muscles means they also grow fat. The recommendation is to pay special attention to children under the age of 11 that play rugby, American football as line men, in heavy weight categories. Application of the latest diagnostic criteria with their actualization on a regular basis, as well as search for additional markers and parameters identifiable in laboratory settings, would ensure adjustment of the athlete's condition in a timely manner.

Keywords: metabolic syndrome, insulin resistance, obesity, arterial hypertension, underage athletes, elite sports, top tier athletes

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МЕТАБОЛИЧЕСКИЙ СИНДРОМ: РИСКИ В ДЕТСКО-ЮНОШЕСКОМ СПОРТЕ

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Метаболический синдром — одно из донозологических состояний, при котором происходят напряжение сразу нескольких систем организма и нарушения во всех видах обмена. Его главные составляющие — висцеральное ожирение, инсулинорезистентность периферических тканей, артериальная гипертензия и неалкогольная жировая болезнь печени. Синдром ассоциирован с риском развития ряда заболеваний, поэтому важно диагностировать его доклинические проявления. Число людей, страдающих избыточным весом и ожирением, только увеличивается, более того, эти состояния активно молодеют. Наличие метаболического синдрома в детском возрасте увеличивает риск развития сердечно-сосудистых заболеваний во взрослом. Высококвалифицированные спортсмены не исключение. Ряд спортивных дисциплин и игровых амплуа способствуют увеличению массы тела. У молодых спортсменов могут быть конституциональные особенности, и мотивирование их к наращиванию мышечной массы без должного контроля приводит к тому, что у них вырастает и объем жировой ткани. Рекомендуется обратить особое внимание на детей в возрасте до 11 лет, занимающихся регби, американским футболом на позициях лайнменов, выступающих в тяжелых весовых категориях. Следование последним диагностическим критериям и регулярное их уточнение, поиск дополнительных маркеров и лабораторных показателей позволят не упустить время и скорректировать состояние спортсмена.

Ключевые слова: метаболический синдром, инсулинорезистентность, ожирение, артериальная гипертензия, несовершеннолетние спортсмены, спорт высших достижений, высококвалифицированные спортсмены

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In the context of sports medicine, metabolic syndrome (MS) is a rather new factor considered. Regular physical activity were believed to largely safeguard athletes from the development of MS. However, the significant and often over-the-top physical strain associated with professional sports is a risk factor for inflammatory processes and oxidative stress, which, in turn, causes endothelial dysfunction and affects the vascular tone regulation [1, 2].

At the same time, in some sports, high results require excessive weight and even obesity (body mass index > 30). Such sports include martial arts (heavy weight category in sumo, judo, sambo, Greco-Roman wrestling), rugby, American football, weightlifting, strongman competition, powerlifting, bobsleigh [2]. These facts, along with the new scientific data obtained in the recent years, dictate the need to revise the previously practiced approaches.

Metabolic syndrome: definition and prevalence

How do experts interpret metabolic syndrome today?
Clinical Guidelines of 2013 by the Ministry of Health of the Russian Federation suggest the following definition: "MS is

characterized by growth of the visceral fat mass, decrease of the insulin sensitivity in peripheral tissues and hyperinsulinemia, which trigger disorders of carbohydrate, lipid, purine metabolism and arterial hypertension (AH) [3].

Some medical professionals consider the spread of MS to constitute a new pandemic; its prevalence exceeds that of diabetes mellitus. According to the WHO Fact Sheet, from 1975 to 2016, the number of obese people worldwide has more than tripled. The prevalence of MS in the population varies from 10 to 30%; in Russia, the figure is from 20 to 35%. Currently, 1.9 billion adults over 18 are overweight, with more than 650 million of them obese. This is 13% of the world's adult population [3–6].

Along with obesity, in adults and adolescents over 16, MS manifests as insulin resistance, dyslipidemia and arterial hypertension [3, 7, 8].

Previously, obesity was considered to be specific to high-income countries, but nowadays it grows increasingly prevalent in low- and middle-income countries. In 2016, about 41 million children under the age of 5 were overweight or obese, while among those older than 5 the conditions were registered in 340 million children and adolescents [3, 9]. Another study states that at least 10–15% of children and adolescents are overweight [6]. In the 0 through 14 years age group, 350 children out of 100,000 in Russia had their first obesity diagnosis, and in the 15 through 17 years age group this figure was almost twice as large almost doubled (708 cases per 100,000 children) [10].

There is an array of diseases associated with obesity, with cardiovascular diseases (CVDs) and diabetes mellitus being the most common thereof. The complications of obesity also include dyslipidemia, non-alcoholic fatty liver disease (NAFLD), reproductive disorders and dysfunctions of the reproductive system, disorders of the musculoskeletal system, obstructive sleep apnea syndrome etc. [7]. Currently, medical professionals and researchers have no univocal view whether these conditions are a complication of obesity or concomitant diseases that, progressing, exacerbate obesity. Nevertheless, many studies have shown that overweight and obesity in children and adolescents are the risk factors for metabolic syndrome, diabetes mellitus and cardiovascular disease later in life. In this connection, early detection and prevention of the metabolic syndrome in children and adolescents is an urgent public health problem [8].

In its work providing comprehensive recommendations for cardiovascular diseases and reduction of risk thereof in children and adolescents, a group of experts has underscored the importance of preventing the development of risk factors (primary prevention) and cardiovascular disease in the future [11].

The recently published data from the study of prevalence of obesity in the population of the Russian Federation (main age groups, duration 1995 through 2019) has shown that on the level of the country's federal districts and constituent entities 15% of children aged 0–14 years are obese, and in the group of 15 through 17 years of age the figure is 7%. At the regional level, the largest proportion of obese children in the 0-14 years age group is in the Kaluga region (37%), Jewish Autonomous Region and Republic of Tyva (35%), and in the 15–17 years age group — Jewish Autonomous Region (14%), Republic of Tatarstan (13%) and Perm region (12%). The incidence of obesity in children aged 0 through 14 years has increased 4 times, from 367.6 per 100,000 population in 1995 to 1417.1 in 2019. Since 2002, the obesity indicator among adolescents aged 15–17 years has grown almost sixfold, which is a matter of great concern; in 2019, it has rapidly increased from 865.1 to 3411.7 per 100,000 population [5].

In 2007, the European regional office of the WHO developed the Childhood Obesity Surveillance Initiative (COSI), which aims to identify the causes of overweight and develop and implement dietary and physical activity guidelines for children of the school age. COSI is one of the largest population-based studies of overweight and obesity in this age group; it includes over 300,000 children from 38 European countries. Its Moscow part took place in 2017–2018 and included 2166 7-year-old children; the study revealed that 27% of boys and 22% of girls were overweight and 10% and 6%, respectively, — obese [12]. These data are consistent with the global trends that indicate both the growing prevalence of these conditions and their increasing registration in younger age groups [6].

Some authors state that the true prevalence of overweight and obesity in children is greater than what is officially reported [13]. They have also shown that childhood obesity is concomitant with poor bone metabolism and imbalanced bone formation and bone resorption processes. An examination of children in the Sverdlovsk region (Russia) has revealed that the prevalence of obesity as registered based on the preventive screenings is significantly higher than what is recorded in the official statistical reports that draw upon the data on people seeking medical assistance willingly. In particular, the prevalence of obesity in children of the 0–14 years age group in the Sverdlovsk region was 18.4% higher than generally in Russia, and for the 15–17 years age group this figure was 9.7% [14].

Diagnostic criteria

In 2007, the International Diabetes Federation (IDF) adopted new age-specific criteria for abdominal obesity and metabolic syndrome in children and adolescents. The criteria dictate diagnosing abdominal (visceral) obesity in the 6–15 years age group if the waist circumference (WC) is equal to or greater than the 90th percentile of the percentile distribution of this indicator. Metabolic syndrome is not diagnosed in the 6–9 years age group, but an obese (visceral obesity) patient with an aggravated family history of MS, type 2 diabetes mellitus, CVD (including hypertension) and/or obesity should be additionally examined and followed-up routinely [15].

In the 10–15 years age group, MS may be diagnosed if, in addition to abdominal obesity, at least two of the following criteria are met: TG ≥ 1.7 mmol/L, HDL < 1.03 mmol/L, BP ≥ 130/85 mm Hg, fasting glucose ≥ 5.6 mmol/L (or type 2 diabetes; Table 1). From 16 years on, the diagnosis of MS is established based on the same criteria as for adults [16].

Along with anthropometric parameters and physiological ranges of blood pressure, puberty significantly alters the fat distribution patterns, which is accompanied by the drop of the adiponectin level and insulin sensitivity by about 30% and additional growth of secretion of this hormone. Such transformations, most pronounced in the pubertal period of development, make interpretation of the laboratory-measured indicators of adolescents a complex matter. This complexity is one of the reasons why medical professionals cannot reach the consensus about what threshold values of certain parameters should be considered signs of MS criteria, especially in the view of differing diagnostic significance and contribution of each of the components [15].

In 2009, experts from the International Diabetes Federation (IDF), the National Heart, Lung and Blood Institute (NHLBI), the American Heart Association (AHA), the World Heart Federation (WHF), the International Atherosclerosis Society (IAS), and the International Association for the Study of Obesity (IASO)

Table 1. Metabolic syndrome criteria for children and adolescents

Age group (years)	Obesity (waist circumference)	Triglyceride level	HDL cholesterol level	Blood pressure (BP)	Glucose level or diagnosed type 2 diabetes
6–9	≥ 90th percentile	Metabolic syndrome is not diagnosed, but family history of MS, type 2 diabetes, dyslipidemia, CVD, hypertension, and/or obesity call for additional examinations			
10–15	≥ 90th percentile (adult criterion if lower)	≥ 1.7 mmol/L (≥ 150 mg/dL)	< 1.03 mmol/L (< 40 mg/dL)	Systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg	≥ 5.6 mmol/L (100 mg/dL) (or diagnosed type 2 diabetes). If ≥ 5.6 mmol/L, an oral glucose tolerance test is recommended
16 and older	Application of the criteria developed by the IDF for adults				

have developed unified criteria for diagnosing MS in adults and adolescents aged 16 and over [16]. These criteria factor in the scientific data accumulated to the moment. The consensus prescribes diagnosing the condition in case at least three of the below-mentioned criteria (Table 2) are met.

The Russian Metabolic Syndrome Clinical Guidelines developed in 2013 note that there are practically no prognostic data substantiating the benefits of various MS diagnosing criteria [3]. In this connection, it is obviously necessary to harmonize and adjust the existing diagnostic criteria for the conditions of the Russian Federation: factor in the ethnic and genetic differences of the Russian population, national nutritional characteristics, lifestyle and economic background in the state. The suggested key diagnostic criterion is the central (abdominal) type of obesity registered at > 80 cm WS in women and > 94 cm WS in men, with a number of additional criteria; the MS diagnosis is considered reliable when the patient exhibits signs of the key criterion and two additional criteria:

– blood pressure level > 140 and 90 mmHg or pharmaceutical treatment of hypertension;

– increased triglyceride levels (≥ 1.7 mmol/L);

– decreased HDL cholesterol levels (<1.0 mmol/L in men; <1.2 mmol/L in women);

– impaired glucose tolerance (IGT) — elevated plasma glucose level 2 hours after loading 75 g of anhydrous glucose with OGTT ≥ 7.8 and < 11.1 mmol/L, provided that the fasting plasma glucose is below 7.0 mmol/L;

– impaired fasting glycemia (IFG) — elevated fasting plasma glucose level ≥ 6.1 and < 7.0 mmol/L, provided that plasma glucose after 2 hours with OGTT is below 7.8 mmol/L;

– combined IFG/IGT — elevated fasting plasma glucose ≥ 6.1 and < 7.0 mmol/L in combination with plasma glucose after 2 hours with OGTT ≥ 7.8 and < 11.1 mmol/L [3].

Abdominal, or visceral obesity should be considered a canonical MS symptom. It has been shown that WC correlates more strongly with visceral adipose tissue than body mass index (BMI). Here, it is important to take into account a fact well-known in sports medicine: BMI depends, interalia, on the type of sport, the athlete's muscle mass and some other factors, which reduces its informativeness as an objective indicator.

A study that included 1037 boys and 950 girls (mean age — 11 years) undertook a stepwise multiple regression analysis of such variables as total cholesterol, triglycerides, high and low density lipoproteins and blood pressure and established that WS is the most significant predictor, regardless of gender [17]. Another study employed dual-energy x-ray absorptiometry (DXA) and showed that it is the WC that allows clear and accurate (87% accuracy for girls and up to 90% for boys) identification of children with low and high body fat mass [18].

In adults, WC is widely used as a diagnostic criterion to judge distribution of fat in the abdominal region, but in children this parameter can be influenced by growth and sexual development, which reduces the accuracy of the visceral adipose tissue assessment. Ethnicity also plays an important role in this context [19].

In 2020, a study that involved 113,453 normal weight children from eight countries (Bulgaria, China, Iran, Korea, Malaysia, Poland, Seychelles and Switzerland) aged 6 through 18 established reference values for the WC percentiles. The researchers have also confirmed that the 90th WC percentile can be used to predict cardiovascular risk in children of normal weight [20]. In 2021, same WC threshold values were recommended in the international consensus made by the experts in the pediatric metabolic fatty liver disease [21].

Metabolic fatty liver is closely associated with obesity, insulin resistance, dyslipidemia and other metabolic constituents of MS; it is often considered the "liver constituent" thereof. Hypertriglyceridemia and MS were shown to be independent factors associated with the development of non-alcoholic steatohepatitis, and hypertriglyceridemia is known to often manifest in top tier athletes, as it supports the body during intense training sessions. In addition to the accumulation of excessive amounts of triglycerides in the liver, induction of oxidative stress plays an important role in the non-alcoholic fatty liver disease (NAFLD) pathogenesis. This kind of stress often emerges against the background of extreme sports-related body overload. According to DIREG 2, a large-scale study, the frequency of NAFLD in Russia in 2007 was 27%, and in 2014 it rose up to 37.1%, which makes this condition the most common liver disease [22].

According to a number of authors, prevalence of NAFLD grows in parallel with the growth of prevalence of obesity

Table 2. MS criteria in adults and adolescents over 16 years of age [16]

MS criteria	Indicators
Abdominal obesity	Critical value exceeded WC based on ethnicity
Triglycerides	> 1.7 mmol/L
HDL cholesterol male female	< 1.0 mmol/L < 1.3 mmol/L
Arterial pressure	≥ 130 / ≥ 85 mmHg
Fasting glucose	≥ 5.6 mmol/L

and MS [23]. An objective assessment is a complex issue, the complexity thereof backed by the limited individual value of the routine liver pathology laboratory diagnostics methods (determination of bilirubin, ALT, AST, g-GT, albumin, ferritin, complete blood count and INR), which are common for outpatient practice. For example, twofold increase of the ALT and AST levels is registered only in 30% of NAFLD patients, and the indicators correlate with the severity of the disease quite weakly. Therefore, this study cannot help establish the prognosis of metabolic steatohepatitis [24]. It is advisable to factor in the influence sports-associated loads have on the ranges of values of indicators measured with laboratory tests. National studies that involved large samples have shown that in sportsmen, reference ranges of the majority of the listed biochemical markers differ significantly from those peculiar to the regular people. Gender differences, and especially age differences, are also of great importance [25].

An analysis of systematic reviews available on PubMed, Scopus and Web of Science yielded 36 prospective studies (5,802,226 patients) that state the association of NAFLD with a moderate increase in the risk of fatal and non-fatal cardiovascular events [26].

Discussing the concept of MS as a complex of conditions predisposing to cardio-metabolic risk factors and the possibility of diagnosing the syndrome in pediatric practice, it is necessary to recognize the fuzziness of the criteria currently applied to children. This fuzziness is the reason behind the wide variation of the assessments of MS prevalence. Thus, in the papers published in 2014–2019 the prevalence of MS was assessed within the range from 0.3 to 26.4%, which, to a certain, is the result of the variety and reliability of the diagnostic criteria used [27].

It is also important to remember that a child, as he/she grows and develops, may meet the applicable criteria at one time and not meet them at another time, and it is not clear whether the recorded changes represent an improvement or deterioration in his/her health status. Nevertheless, there is conclusive evidence that childhood MS and childhood overweight are associated with a greater than 2.4-fold risk of developing MS in adulthood, and the possible future condition can be predicted from the age of 5 years [28]. A certain conformation of this statement can be found in a study that demonstrated the relationship between childhood MS and cardiovascular diseases in adults 25 years later [29].

As an individual component of MS, arterial hypertension has a number of clinical peculiarities in its course. The said peculiarities include frequently observed development of refractory hypertension, early damage to target organs, such as the development of left ventricular hypertrophy that quickly leads to myocardial dysfunction, renal hyperfiltration, decreased elasticity of the aorta and arteries. According to the ABPM data, hypertension patients with metabolic disorders, compared to hypertensive patients without such, are diagnosed with more pronounced disturbances in the blood pressure's circadian rhythm, higher rates of pressure load at night and increased variability [3].

According to some researchers, screening of children and adolescents for overweight and obesity should be complemented with screening for high blood pressure [30]. It is fairly well known that BP levels in children and adolescents are closely associated with age, sex, and body length. However, the wide variety of anthropometric data seen even within one age group, as well as gender differences, substantiate the need to use special centile tables based on the results of the relevant population (national) studies [31].

A 2016 study that involved not overweight children and adolescents aged 6–17 years from seven countries (China, India, Iran, Korea, Poland, Tunisia and USA) established the international reference BP percentiles depending on sex, age and height. These international reference BP values were taken as criteria for comparison of prevalence of elevated BP in children and adolescents [32]. In the same 2016, Russian cardiologists prepared clinical guidelines for arterial hypertension diagnosing and treatment in children and adolescents, which suggest using centile tables as criteria for assessing blood pressure values and factor in age, gender and height [33].

In September 2022 there was published a consensus prepared by a number of European associations that covered hypertension in children and adolescents. This paper recommended measuring blood pressure and interpreting the results taking into account the centile values for age, sex and height, and provided the criteria for assessing modifiable risk factors, including overweight, obesity, dyslipoproteinemia, hyperglycemia, and insufficient physical activity [34]. However, none of the above international and domestic consensus documents grades children's BP values factoring in their sports activities, although many millions of children and adolescents go in for sports worldwide. Moreover, various studies have convincingly shown the significant impact of excessive (professional) sports load on systemic blood pressure and the subsequent high risk of violations of its regulation, which can ultimately cause arterial hypertension and other cardiovascular events.

To a certain extent, the expediency of BP control and early detection of AH as an early marker of MS is confirmed by the data on pathophysiological role of insulin resistance and hyperinsulinemia in the development of endothelial dysfunction brought by an imbalance in the synthesis of vasodilators and vasoconstrictors, with subsequent development of hypertension [35, 36].

Many different markers synthesized in the body adipose tissue correlate with metabolic and cardiovascular risk factors; in particular, such are pro-inflammatory cytokines (TNFα, IL6) and adipokines (eg, adiponectin, leptin, chemerin). Measuring the level of of most of these adipokines is not yet part of routine laboratory examinations, however, a number of researchers suggest testing for adipokines and inflammatory markers in the context of basic examination of obese children and adolescents to assess the risk of cardio-metabolic diseases.

Only a few works describe the relationship between age, gender, specifics of pubertal development and the level of adiponectin in childhood. For example, the level of adiponectin in children was found to be higher than in adults, but during puberty it goes down significantly. It has also been shown that in children, adiponectin is negatively correlated with the body fat percentage, and significant weight loss during treatment of obesity is associated with the growing level of adiponectin and improving insulin resistance. This correlates with the results of studies in adults that describe the close relationship between adiponectin and body fat and insulin resistance [37].

A number of papers highlight the high percentage of detection of metabolic disorders and overweight, up to obesity, in young American football players. It should be noted that the desire to gain more muscle mass for a certain role on the field, which is typical for professional players, is not considered to be a significant risk factor, since young athletes, college students, do not have a clear role and change it during the season. Still, according to the surveys involving national samples, overweight and obesity are the conditions registered in them 45% and 42% more often, respectively [2, 38].

Compared to the general population, young rugby players (aged 9–14) in France, Europe grow overweight and obese more often. The conducted balance studies confirmed it is the high mass of fat, not muscle, that is the primary cause of overweight in young athletes [39].

Overweight and obesity pose more risks for the health of young athletes than only the risk of MS. Several meta-analyses and original studies provide evidence that these conditions make young athletes more prone to trauma. Development of inflammatory reactions to injury is an important aspect, as proven by the high values of a number of cytokines (TNFα, IL1, IL6) and such markers as CRP and fibrinogen, which correlate with a high risk of obesity. The role of inflammatory reactions and endothelial dysfunctions, which, as mentioned above, are peculiar to MS, disallows excluding formation of a certain vicious circle brought by injuries in overweight athletes, this circle ultimately undermining both the athlete's health and his/her sports performance [6, 30, 40].

Discussion of the pathophysiological processes that condition development of MS necessitates recalling the hypothesis of chronic stress. Studies of different years allow a high degree of certainty in considering the physiological role nonspecific chronic stress reaction plays in energy support of specific adaptive components. One of such studies suggests differentiating between energy-tropic and trophotropic stages of chronic stress, with further subdivision of the stages into phases: intense adaptation, relative compensation, and decompensation [41]. The energy-tropic stage, diagnosed, for example, in children with intrauterine malnutrition, as well as in older children and adults, often transforms into the trophotropic stage, which is accompanied by the development of obesity, diabetes mellitus, CVD and especially often — arterial hypertension. According to many researches, the latter group of diseases constitutes the metabolic syndrome. Thus, this hypothesis suggests interpreting MS as a trophotropic stage of chronic stress [42, 43]. It should be noted that young athletes undergo significant pubertal transformations that make them especially vulnerable to the negative impact of stress factors. However, the results of studies investigating the relationship between MS, chronic stress and sports loads have not yet been published.

CONCLUSION

The problem of MS is obviously relevant to the sports medicine; further targeted research is needed to develop diagnostic criteria for this condition and methodological approaches to its management tactics applicable to children and adolescents, such criteria and approaches factoring in not only age and gender differences but also the specifics of the practiced sport through the lens of pubertal development. The results of such research would allow adjusting the MS diagnostic algorithm proposed in the literature to the characteristics of children and adolescents involved in sports, with the appropriate standard and reference values of the parameters that, as a rule, are looked into as part of in-depth medical examinations. Practical implementation of this algorithm can fundamentally improve the quality of early diagnosis and treatment and prevention programs developed for this syndrome.

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