METABOLIC SYNDROME A WIDESPREAD THREATENING CONDITION; RISK FACTORS, DIAGNOSTIC CRITERIA, THERAPEUTIC OPTIONS, PREVENTION AND CONTROVERSIES: AN OVERVIEW

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METABOLIC SYNDROME A WIDESPREAD THREATENING CONDITION; RISK FACTORS, DIAGNOSTIC CRITERIA, THERAPEUTIC OPTIONS, PREVENTION AND CONTROVERSIES: AN OVERVIEW (Abstract): Metabolic syndrome diagnostic criteria include at least three of five of the following medical conditions: abdominal obesity, high blood pressure, abnormal high fasting plasma glucose, elevated serum triglycerides and low HDL (high density cholesterol) level. Sedentary, overweight and obesity are characteristically associated with the syndrome, nevertheless there are new studies which indicate that chronic stress, through deregulation of the hypothalamic-pituitary-adrenal (HPA) axis is also involved in the development of the syndrome. Metabolic syndrome represents a significant risk for the development of the cardiovascular diseases. New studies in the USA have estimated its prevalence at approximately 34 % of the adult population and its prevalence is increasing with age. Diagnosis guidelines are establishing the metabolic syndrome diagnostic when are met three of the following five conditions: fasting glucose ≥ 100 mg/dL or type 2 diabetes receiving drug therapy for hyperglycemia; high blood pressure ≥ 130/85 mm Hg or high blood pressure receiving drug therapy; triglycerides ≥ 150 mg/dL or treatment for plasma hyper-triglyceride value; HDL-C < 40 mg/dL in men and < 50 mg/dL in women or if under therapy for reduced HDL-C levels and waist circumference of ≥ 102 cm in men and ≥ 88 cm in women. Besides important change of lifestyle, often drug therapy is needed (diuretics and ACE inhibitors, cholesterol drugs and weight loss medications). The value of physical activity and diet in prevention and treatment of the syndrome is supported by numerous studies. Association of metabolic syndrome and cardiovascular risk is still a matter of controversy, in what concerns the lack of significant cardiovascular risk in the case of obesity itself without metabolic syndrome. Keywords: METABOLIC SYNDROME, OBESITY, HPA (HYPOTHALAMIC-PITUITARY-ADRENAL) AXIS, HDL CHOLESTEROL, LDL CHOLESTEROL

Metabolic syndrome is a disorder affecting the energy use and storage. Criteria needed for diagnosis are including at least five of the following medical conditions: abdominal obesity, high blood pressure, abnormal high fasting plasma glucose, elevated serum triglycerides and low HDL (high density cholesterol) level. Metabolic syndrome represents a significant risk for the development of cardiovascular diseases and diabetes. Different studies have estimated the prevalence of the syndrome in the USA at approximately 34 % of the adult population (1, 2).
Metabolic syndrome is also known as: insulin resistance syndrome, syndrome x, metabolic syndrome x, cardio metabolic syndrome. The term of metabolic syndrome was first used in the late 1950s and became commonly used at the end of 1970s, first to describe association of risk factors for diabetes (3). In 1947 it was first noticed that the upper body obesity was predisposing to diabetes, atherosclerosis and gout. In 1977 was used the term of metabolic syndrome to describe the association between obesity, diabetes mellitus, hyper-lipoproteinemia, hyperuricemia and hepatic steatosis and thus to contour the risk factors for atherosclerosis (2, 4).

**RISK FACTORS**

New researches are indicating that chronic stress is involved in the development of the metabolic syndrome, by disruption of the hormonal balance of the hypothalamic-pituitary-adrenal axis (HPA-axis). Disruption of HPA-axis induces increased circulatory cortisol levels with consequently high glucose and insulin levels, finally leading to insulin-triggered effects on adipose tissue and resulting into visceral adiposity, insulin resistance, dyslipidemia, high blood pressure and effects on bone metabolism, with the development of “low turnover” osteoporosis. Disruption in the functioning of HPA-axis is explaining the involvement of the abdominal obesity in the development of the cardiovascular disease, type 2-diabetes and stroke (5).

Overweight and obesity is the main characteristic of the syndrome, reflected in the strong link between its prevalence and waist circumference, associated with increasing adipose mass. Nevertheless, there are cases which show normal weight but do have the syndrome (6). Sedentary behavior is one of the main risk factors for cardiovascular diseases and mortality. Most of the metabolic syndrome’s features are associated with sedentarism: increased abdominal adipose tissue, low HDL cholesterol level, high blood pressure, high glucose levels (7).

Metabolic syndrome affects 44% of the US population over 50 years of age. The syndrome is more frequent in female sex and its prevalence is increasing with age, all over the world. Metabolic syndrome is increasing five folds the risk of type 2 diabetes mellitus, which is seen like a complication of the syndrome. It is believed that pre diabetes and metabolic syndrome are representing in fact the same disorder, but defined by different sets of biological markers. Metabolic syndrome is associated with a higher risk for cardiovascular disease, than the cases with type 2 diabetes mellitus without associated metabolic syndrome. Hypoadiponectinemia is increasing insulin resistance and it represents also a risk factor for the development of the metabolic syndrome.

Patients with schizophrenia and other psychiatric diseases are at high risk for metabolic syndrome, a risk which is increased in such cases by sedentary behavior, noxious dietary habits and antipsychotic drug – induced adverse effects. 32 to 51% of individuals with psychiatric disorders have metabolic syndrome, with a higher prevalence in women than in men (2, 8). Common triggers, such as excessive sugar intake and generally overabundant food environment are incriminated in the concomitant development of multiple metabolic abnormalities at the same time, pointing once more the dysfunction of energy use and storage paths in the metabolic syndrome (8, 9, 10).
Markers of systemic inflammation, such as C-reactive protein, fibrinogen, interleukin 6, tumor necrosis factor alpha (TNF-α) are increased in the metabolic syndrome. TNF-α is causing the production of inflammatory cytokines and is inducing cell signaling through interaction with TNF-α receptor, which may lead to insulin resistance. Increase of adipose tissue is increasing the number of immune cells inside it, cells which are involved in the chronic inflammatory processes; chronic inflammation being a risk factor for the development of arterial hypertension, atherosclerosis and diabetes (11).

**DIAGNOSTIC CRITERIA**

Main symptom of metabolic syndrome is the central obesity (also-known as visceral, male-pattern or apple-shaped adiposity) – an overweight with accumulation of adipose tissue mainly around the waist and trunk (6). Signs of metabolic syndrome include: high blood pressure, decreased fasting serum HDL cholesterol, elevated fasting serum triglyceride level (VLDL triglyceride), impaired fasting-glucose level and insulin resistance. Metabolic syndrome is usually associated with hyperuricemia, hepatic steatosis, polycystic ovarian syndrome in women and erectile dysfunction in men, and acanthosis nigricans, xanthomas or xanthelasmas, in patients with severe dyslipidemia (12).

The diagnosis guidelines from National Heart, Lung and Blood Institute (NHLBI) and the American Heart Association (AHA) are stipulating that the diagnosis of metabolic syndrome is established, when are met three of the following five conditions (13):
- Fasting glucose ≥ 100 mg/dL or type 2 diabetes which is receiving drug therapy for hyperglycemia;
- Blood pressure ≥ 130/85 mmHg or high blood pressure which is under drug therapy;
- Triglycerides ≥ 150 mg/dL or if treated for hypertriglyceridemia;
- HDL-cholesterol < 40 mg/dL in men and < 50 mg/dL in women, or if under therapy for reduced HDL-cholesterol;
- Waist circumference ≥ 102 cm in men, or ≥ 88 cm in women.

Complaints of chest pain, dyspnea or claudication are frequent symptoms of potential complications. Obstructive sleep apnea seems to be a novel risk factor for metabolic syndrome (14).

A matter of controversy is represented by the fact that adipose tissue and resulted obesity are generally explaining most of the cardiovascular risk. Nevertheless, obesity itself, without metabolic syndrome is not associated with a significant cardiovascular risk, while metabolic syndrome without obesity is associated with a significant risk of cardiovascular disease and diabetes.

Generalized lipodystrophy characterized by an almost complete absence of adipose tissue develops signs of metabolic syndrome in the absence of adipose tissue, resulting in type 2 diabetes. Type 2 diabetes is cured if in transgenic mice with lipodystrophy, adipose tissue is transplanted (15, 16).

**THERAPEUTIC OPTIONS AND PREVENTION**

Change of lifestyle is the first choice treatment of the metabolic syndrome. If the efforts of reversing the risk factors are not giving expected results in 3 to 6 months, then drug therapy is needed. Diuretics and ACE inhibitors are used to treat arterial hypertension. Cholesterol drugs are used to
reduce LDL cholesterol and triglycerides elevated levels and to increase HDL low levels. Sometimes are used weight loss medications, which may result in weight loss.

As obesity is generally considered the main feature of the syndrome which is leading to the development of the other symptoms, weight loss as well as lifestyle changes, including diet and physical activity, may reduce the need for medications. Many studies are supporting the value of physical activity and diet in the therapy of the metabolic syndrome. Restriction of the total dietary carbohydrate intake shows most efficiency in decreasing common manifestations of the metabolic syndrome. Unfortunately, high-dose statins therapy has been resulted in rapid progression to diabetes (17).

Different strategies are used to prevent the development of the metabolic syndrome, like increased physical activity (for example walking 30 minutes daily) and low caloric diet. International Obesity Task force is supporting the idea of a need for sociopolitical measures to decrease the rate of metabolic syndrome development in population. Caerphilly Heart Disease Study which followed 2375 male subjects over 20 years suggested that daily intake of approximately 568 ml of milk or correspondent dairy derivatives reduced with more than 50 % the risk of metabolic syndrome. There are studies which support these findings, while others are questioning them (7, 18, 19).

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**NEWS**

**ONCOPLASTIC MAMMOPLASTY ASSOCIATED WITH POSTMASTECTOMY RADIATION THERAPY: THE PLAN FOR REDUCING RECONSTRUCTIVE COMPLICATIONS**

It is widely accepted that breast cancer patients who require radiation therapy after mastectomy and immediate reconstruction treatment, suffer high complication rates. A group of researchers from University of California showed that combining neo-adjuvant chemotherapy with oncoplastic mammoplasty is one of the best solutions for high aesthetics results with low local recurrence rates for patients needing radiotherapy treatment after surgery. 64 patients mastectomized with immediate reconstruction were compared with 37 who underwent the new procedure. After using the Fisher’s exact test, the results showed rates of complications for infection 16.2% versus 35.9% (p < 0.04), for skin flap necrosis 10.8% versus 29.7% (p < 0.05) and for unplanned intervention 2.7% versus 37.5% (p < 0.001), much higher for the mastectomy group (excepting seroma – 7.8% versus 5.4%, p = 0.6). The authors show that oncoplastic mammoplasty is highly recommended to patients with local tumor in advanced stages, in order to avoid complications of multiple long lasting surgical procedures, improving quality of our patients’ life. (Peled AW, Sbitany H, Foster RD, Esserman LJ. Oncoplastic mammoplasty as a strategy for reducing reconstructive complications associated with postmastectomy radiation therapy. Breast J 2014; 20(3):302-7)