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*Jarosław Kozakowski

Obesity and musculoskeletal system

Otyłość a układ mięśniowo-szkieletowy

Department of Endocrinology, Centre of Postgraduate Medical Education, Bielański Hospital, Warsaw
Head of Department: Professor Wojciech Zgliczyński, MD, PhD

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S u m m a r y

Obesity called "tsunami of the 21st century" leads to the development of many metabolic disorders and diseases and is a cause of increased morbidity and mortality. On the other hand, diseases of the musculoskeletal system are now the main cause of disability and the second cause of doctor visits.

With many epidemiological studies, it is clear that excessive body weight adversely affects the course of almost all diseases of the musculoskeletal system, such as osteoarthritis, metabolic diseases, e.g. osteoporosis or gout, connective tissue diseases – rheumatoid arthritis, systemic lupus erythematosus, rare diseases like idiopathic hyperostosis, or rarely diagnosed as fibromyalgia. Although in many cases the relationship between the increasing weight and the course of the musculoskeletal system diseases is confirmed only on the basis of observational and epidemiological studies, and the mechanisms of the destructive impact of obesity on musculoscelestal system remain unexplained it is considered that they are complex, and include the biomechanical, diet, genetic, inflammatory and metabolic factors. In many cases not only the increase in body weight seems to have a meaning but also its nature: whether it relates to fat mass, or lean body mass, including skeletal muscles. A large role in etiopathogenesis of the musculoskeletal system changes under the influence of obesity seem to play adipokines and proinflammatory cytokines – products of changed fat tissue.

A huge spread of both obesity and diseases of the musculoskeletal system requires knowledge by doctors of their mutual relations.

S t r e s z c z e n i e

Otyłość nazywana „tsunami XXI wieku" prowadzi do rozwoju wielu zaburzeń metabolicznych i chorób, będąc przyczyną zwiększonej zachorowalności i umieralności. Z drugiej strony, choroby narządu ruchu są obecnie główną przyczyną niepełnosprawności i drugą co do częstości przyczyną wizyt u lekarza. Z wielu badań epidemiologicznych jasno wynika, że nadmierna masa ciała wpływa niekorzystnie na przebieg niemal wszystkich chorób układu mięśniowo-kostnego, od choroby zwyrodnieniowej stawów, poprzez choroby metaboliczne (m.in. osteoporoza, dna moczanowa), tzw. choroby układowe tkanki łącznej (reumatoidalne zapalenie stawów, toczeń rumieniowaty układowy), aż po choroby rzadkie (np. idiopatyczna hiperostoza) czy rzadko rozpoznawane (np. fibromialgia). Choć najczęściej zależność między wzrostem masy ciała a przebiegiem chorób układu ruchu potwierdzona jest badaniami obserwacyjnymi i populacyjnymi, a mechanizmy destrukcyjnego działania otyłości na układ mięśniowo-kostny pozostają wciąż niewyjaśnione, to uznaje się, że mają one charakter złożony i obejmują wpływ czynników biomechanicznych, dietetycznych, genetycznych, zapalnych i metabolicznych. W wielu przypadkach wydaje się mieć znaczenie nie tylko sam wzrost masy ciała, ale także jego charakter: czy dotyczy on masy tłuszczu, czy beztłuszczowej masy ciała, w tym mięśni szkieletowych. Dużą rolę w etiopatogenezie zmian w układzie mięśniowo-kostnym pod wpływem otyłości zdają się odgrywać produkty zmienionej tkanki tłuszczowej – adipokiny i cytokiny prozapalne.

Ogromne rozpowszechnienie zarówno otyłości, jak i chorób układu ruchu wymaga poznania przez lekarzy ich wzajemnych relacji.

Conflict of interest
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Address/adres:
*Jarosław Kozakowski
Department of Endocrinology
Centre of Postgraduate Medical Education
Bielański Hospital
ul. Cegłowska 80, 01-809 Warszawa
tel. +48 (22) 834-31-31
fax +48 (22) 834-31-31
jkozakowski@cmkp.edu.pl

DEFINITION AND DIAGNOSING OF OBESITY

World Health Organization (WHO) defines overweight and obesity as abnormal or excessive fat accumulation that present a risk to health (1). "Algorithms of diagnosis and treatment of endocrine diseases" prepared by Polish Society of Endocrinology define

obesity as a chronic illness, characterized by excessive fat accumulation, which increases the risk of many social diseases, including cardio-vascular or metabolic ones and cancers (2). Obesity is currently the most common metabolic disease all over the world, according to WHO reaching an epidemic size and posing a key health problem in developed and developing countries (3). Obesity is measured with BMI index, calculated as a body weight multiplied by body height squared (kg/m^2). BMI equal to or higher than 30 kg/m^2 indicates obesity, and over 40 kg/m^2 is considered as morbid obesity. Depending on the location of excessive fat tissue obesity can be classified as abdominal (central), gynoid or mixed one.

Obesity is a key element of the so-called metabolic syndrome (MS). For example: MS criteria as defined by International Diabetes Federation (IDF) include: abdominal obesity (female waist > 80 cm, male waist > 94 cm), and at least two symptoms of the following:

- fasting blond glucose ≥ 100 mg/dL (5.6 mmol/L),
- triglyceride level ≥ 150 mg/dL (1.7 mmol/L),
- HDL-C cholesterol in male < 40 mg/dL and female < 50 mg/dL,
- blood pressure ≥ 130/85 mmHg.

In 2014 an estimated 1.9 billion of people over eighteen were overweight, and 600 million were obese. In other words: 13% of the world population were obese (11% males and 15% females). In 1980-2014 the number of obesity cases increased more than twice (1). An increasing number of obese children and young people is of particular concern.

The number of overweight or obese people in Poland is presented in table 1 (4).

Tab. 1. The number of overweight and obesity cases in Poland (4)

Study	Males		Females	
	Overweight and obesity (%)	Obesity (%)	Overweight and obesity (%)	Obesity (%)
"Household Food Consumption and Anthropometric Survey", IŻŻ, 2000	56.7	15.7	48.6	19.9
NATPOL, 2002	58	19	48	19
WOBASZ, 2003-2005	61.1	21.1	48.6	22.4
NATPOL, 2011		~ 25		
GUS, 2004	52.1	12.6	39.1	12.5
GUS, 2011	61.4	16.6	44.6	15.2

Obesity is a direct cause of many metabolic disturbances and disorders. It constitutes a basic element of metabolic syndrome, adds to development of insulin resistance, type 2 diabetes, hypertension, dyslipidemia, and consequently arteriosclerosis, non-alcoholic fatty liver disease, cardiovascular disease and stroke. Obesity is also connected with sleep apnea, cholelithiasis, infertility (women) and erection problems (men) and constitutes a risk factor in many types of cancer, e.g. oesophagus, endometrial, breast or colon cancer.

OBESITY AND THE MUSCULOSKELETAL SYSTEM

It is believed, that the relationship between obesity and musculoskeletal diseases is complex, involving biomechanical, dietary, genetic, inflammatory, and metabolic factors. Excess body weight has long been claimed to be related to many symptoms and diseases of muscles and bone. These are presented in table 2.

Tab. 2. Relationship between obesity and symptoms and diseases of musculoskeletal system (5)

Symptoms and diseases of musculoskeletal system related to obesity
– degenerative disease (knees, hips, palms) – spinal pain – diffuse idiopathic skeletal hyperostosis – gait disturbances – soft tissues illnesses (e.g. carpal tunnel syndrome, plantar fasciitis) – osteoporosis – gout – fibromyalgia – connective tissue diseases (rheumatoid arthritis, systemic lupus erythematosus)

Osteoarthritis (OA) is the most common skeleton disease. Numerous epidemiological studies indicate a clear relation between BMI and the development of degenerative changes, evaluated both clinically and with an x-ray (6, 7). The odds ratio (OD) for the development of degenerative changes in knees for BMI increased by 5 units is 1.6 (8). In a study of twins it was proven that an increase of body weight by 1 kg leads to increased risk of radiological changes in knee and interphalangeal joints (9). The impact of obesity on the development of osteoarthritis, which is visible in many joints, e.g. hips, palms, patellofemoral and others indicates a share of both mechanical and metabolic factors in their etiopathogenesis. These factors have not been well recognized so far, however, an increased amount of cartilage oligomeric matrix protein (COMP) and the products of collagen type 2 degradation in joint cartilages of obese people were found (10). Those with osteoarthritis were also found to have leptin (cytokine coming from fat tissue) in the synovia. Its quantity indicated a correlation with BMI. Leptin was also found in cartilages and osteophytes (5). Current research which MRI scan helps to image the relation between body composition and the condition of cartilage. A study with MRI and densitometry proved for instance a positive correlation between muscle weight and the thickness of cartilage of the tibia. Such correlation was not found for fat weight (11). Also a correlation between body weight and the degree of damage of cartilage was found. Studies of activity of destructive factors indicate that the damage to cartilage in obese people precedes the occurrence of radiological symptoms of osteoarthritis. Excess body weight is also a strong prognostic of the development of changes in joints. The impact of obesity on joint structures may

depend on the placement of bone structures. E.g. varus malalignment of femurs increases the effect of excess body weight on knees, while valgus malalignment of bones are not so affected by obesity (12). Also exercise is an important factor. It must be borne in mind that in physiological conditions the pressure on knee joint cartilages while walking is about three times as high as normally. Running or walking upstairs mean the pressure increases 6-10 times. It is obvious that in obesity such loads must be particularly destructive.

Another common musculoskeletal problem is back pain. The studies on the impact on such symptoms are unclear, although excess body weight seems to add to a higher exposure to radical pain and the occurrence of neurological symptoms. Also the chronic character of pain seems to be related to BMI increase (13). In a group of physically working middle-aged men it was proven with MRI that overweight is related to lowering the signal from nucleus pulposus, however, it has not been established if the symptom is related to clinical symptomatology (14). It was found that in obese patients fat tissue could expand within dura matter, which can lead to stenosis of the spinal canal (15). On the other hand cervical and lumbar spine pains as well as foot pains were proven to diminish after a significant reduction of body weight following a bariatric surgery (16).

A diffuse idiopathic skeletal hyperostosis occurs much more rarely than back pain. The illness is characterized by bone hypertrophy in the connections of ligaments, aponeuroses, synovial capsules. Changes are particularly visible in dorsal vertebrae, where large pseudo-spurs similar to parrot's beaks, usually including several vertebrae. Also some changes within inner table of the frontal bone were noticed. Although etiopathogenesis of the diseases has not been well recognized, it was found to occur more often in patients with a high BMI (17). Also the leptin levels in people with idiopathic skeletal hyperostosis is higher than in general population (18). However, the role of this adipokine in the development of changes in periarticular tissues is not known.

The impact of obesity on gait is negative. Excess body weight results in the flattening of natural arches of the feet, and while walking – in excess movement of heel, which leads to excess abduction of the anterior foot. Also the foot joint may be overloaded. The whole posture changes, becomes less stable, with the body leaning too much (19). Morbid obesity also slows down movement, and significantly changes walking distances. It was proven that effective reduction of body weight combined with balance exercising helps regain gait stability.

Obesity adversely affects the functioning and structure of soft tissue related to the motor organ. In a 5-year prospective observation it was found that excess body weight increases the risk of tendonitis related to the work performed (20). Many studies showed that obesity is an important factor which adds to the development of the carpal tunnel syndrome; for instance, an analysis of data obtained from general practitioners in the UK helped to establish the risk factor (OR) in such cases at 2.06 (21). Also the frequency of plantar fasciitis shows a correlation with obesity. The risk factor (OR) of unilateral inflammation increases to 5.6 when compared to people with proper BMI (22).

Numerous observations indicate a positive correlation between BMI and bone mass. It is observed for both sexes, although it is most visible in post-menopausal women (23, 24). The authors of one of the papers calculated that a 10-kilogram increase in body weight is related to an improvement in bone mineral density (BMD) by 1% (25). The mechanisms explaining the correlation include intensified aromatization processes in a larger volume of fat tissue, with a subsequent increase in the pool of estrogens, the hormones which are a key factor in maintaining bone mass. Also the mechanical effect plays a part, i.e. an increase in pressure forces on bones resulting from an increased body weight. This helps to stop apoptosis, and stimulates proliferation and differentiation of osteoblasts and osteocytes following an activation of Wnt/β-catenin signal and inhibition the expression of PPARγ receptors (26). It is generally claimed that there is a strict correlation between the control of energy balance of the body and bone homeostasis by control centers in the central nervous system (CNS). Such coordination is possible because of the functioning of the mechanisms integrating signals generated in the CNS, and the signals coming from peripheral organs. The latter type of regulation is effected with mediators such as leptin or adiponectin. For example, releasing leptin following the expansion of fat tissue results in afferent adrenergic activity on the one hand, and stimulating receptors β2 adrenergic in osteoblasts on the other hand, which results in intensified process of bone resorption and stopping osteogenesis (27). Thus hyperleptynemia should be deemed a negative regulator of bone mass. Also proinflammatory cytokines released from the changed fat tissue in obese people, such as TNF-α, Il-1 or Il-6 are important mediators of differentiation of osteoclasts and bone resorption. They stimulate the activity of osteoclastic cells through the regulation of RANKL/RANK/osteoprotegerin system (28). On the other hand, adiponectin may affect the bone directly and indirectly, inhibiting the bone synthesis or the influence of adrenergic activity from the central nervous system, respectively. Studies on animals showed that adiponectin may inhibit osteoclastogenesis, slow down the bone resorption and consequently increase BMD (29). Finally, a negative effect of a diet rich in fat on absorption of calcium from the digestive tract should be considered. The phenomenon is all the more significant because the obese have been found to have a considerably lower concentration of vitamin D, i.e. the factor responsible for absorbing substrates for bone synthesis from the digestive tract.

Although obesity is commonly believed to protect from osteoporosis, it must be borne in mind that the

increased fat volume in bone marrow can have an adverse effect. Moreover, recently published studies suggest that a protective role of a large body weight is more related to higher muscle weight than the increased fat volume. An increase in fat weight turns out to be a factor which quickens the decrease of BMD when an analysis considers the elements of body composition. Some observations also claim that the type of obesity is of importance: abdominal obesity is bad, and excess subcutaneous fat tissue does not adversely influence body mass (27).

The influence of obesity on the risk of bone fractures has not been precisely defined yet, and research provides ambiguous results (30, 31). A recently presented study of 429 obese women after menopause (BMI 50-83 kg/m^2) indicated that BMD in this group is higher and the frequency of fractures lower than in slim women (32). A meta-analysis of large epidemiological studies shows that obesity is more or a factor decreasing a risk of bone fracture. On the other hand, an observation of a group of older men (Osteoporotic Fractures in Men – MrOS) indicated that an increase in BMI is a risk factor in some fractures (33). Also patients with type 2 diabetes are more often found to suffer from bone fractures, despite appropriate or even slightly higher BMD values than healthy ones (34). In a recently published trial (35) in 68 postmenopausal women with type 2 diabetes a similar prevalence of low-trauma fractures was observed as in 72 healthy controls in contrast to normal BMD in diabetic patients. Women with diabetes had significantly higher trunk fat % and significantly lower legs lean mass % and legs fat mass %. Legs lean mass % was significantly lower in fractured diabetic group and negatively correlated with glycaemia and HbA1c. Authors conclude that abdominal obesity and decrease in muscle mass may contribute to low bone formation in women with type 2 diabetes. Further research is needed to determine whether maintenance of muscle mass, especially in the lower extremities and/or reduction of central fat mass can prevent fractures in diabetic patients.

Excess body weight is one of recognized factors of etiopathogenesis of gout. It is known that concentration of uric acid in blood shows a direct correlation with BMI value (36). The volume of fat is a significant determinant of hiperuricemia and lowering clearance of uric acid.

Fibromyalgia is pain syndrome of unknown etiology, characterized by chronic, generalized muscle – joint pain and tenderness in typical points. According to criteria by American College of Rheumatology in order to diagnose an illness the following should be indicated:

- lateral pains,
- over and below waist,
- at least for 3 months,
- covering at least 11 points out of 18 (9 pairs).

The illness occurs 8 x more often in women, most often 35-55 years old. Although its etiopathogenesis is probably heterogenous, obesity is believed to be one of factors adding to its development. Conversely, reduction in body weight obtained either after a life style change or bariatric surgery leads to lesser pain, clinic improvement and better life quality (37).

The most common illness in the group of the systemic connective tissue diseases is rheumatoid arthritis (RA). It was proven that one of risk factors of this disease is BMI > 30 kg/m^2 (38). Excess body weight also decreases the quality of life of RA patients. The role of obesity in RA etiopathogenesis is not clear, but an increased concentration of some adipokins (leptines, visfatin, adiponectin) suggests their participation in the mechanism of chronic inflammation, which is the core of the illness (39). Obesity also often accompanies systemic lupus erythematosus (SLE), although in that case it does not seem to take part in development of hypertension or diabetes, nor does it adversely influence the quality of life of SLE patients (40).

Considering the relationship between obesity and the development and further course of many illnesses of musculoskeletal system excess body weight adds to progressing disability of the patients. The condition is often linked with intensified back pain and pain in lower limb joints, i.e. knees and hips. The disabled have been found to be in obese 2.5 times as often as in their able slim counterparts (41). On the other hand obesity leads to limited physical ability both sub and maximal one. Reduction in body weight in such cases usually leads to increased mobility and lowered pain felt by patients.

In conclusion: obesity is now considered a tsunami of the 21st century, and the musculoskeletal system diseases are most often diagnosed by doctors. They are the first reason for disability and the second most frequent cause of appointments with basic health care doctors. As was shown in many other epidemiological studies and observations, excess body weight constitutes a risk factor and worsens the course of many musculoskeletal system illnesses, although the mechanisms underlying these correlations still remain to be explained. Studies aimed at their defining will help to develop effective strategies of prevention and treatment of both these important problems of modern medicine.

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