

# Obesity in rheumatological practice

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## Abstract

Obesity is a chronic disease that leads to the development of secondary metabolic disturbances and diseases and strongly contributes to increased morbidity and mortality. On the other hand, musculoskeletal disorders are currently the main cause of disability and the second most frequent reason for visits to the doctor. Many studies clearly show that excessive body weight adversely affects the course of almost all musculoskeletal system diseases, from osteoarthritis, through metabolic, systemic connective tissue, to rarely diagnosed diseases. The impact of increased fat mass on the musculoskeletal system is presumably complex in nature and involves the influence of biomechanical, dietary, genetic, inflammatory and metabolic factors.

Due to the epidemic nature of obesity and its serious health consequences, this disease requires energetic treatment. It is always based on lifestyle modification enriched, if necessary, by pharmacological and, in justified cases, surgical treatment.

**Key words:** obesity, osteoarthritis, osteoporosis, musculoskeletal system.

## Introduction

Obesity is defined as a chronic disease associated with abnormal or excessive fat accumulation that leads to the development of secondary serious metabolic disturbances and diseases. Excessive body weight has become a major public health problem especially in developed and developing countries. According to a World Health Organization (WHO) report more than 1 billion people worldwide are obese – 650 million adults, 340 million adolescents and 39 million children [1]. In Poland in 2020, 54% of inhabitants were overweight. The prevalence of obesity was estimated at 10% [2].

Increased body mass index (BMI) has been identified as a risk factor for the symptoms of musculoskeletal system disorders. These disorders may trigger pain, affect joint mobility, lead to postural changes and contribute to physical incapacities and reduced quality of movements. Currently musculoskeletal disorders are the main causes of disability and pain worldwide, especially in industrialized regions [3].

Although a causative relationship between excess body weight, particularly fat mass, and musculoskeletal

problems is difficult to establish for many conditions, there is abundant scientific evidence on the role of obesity in the etiology of locomotor system diseases. On the other hand, it has also been proved that early therapeutic intervention based on lifestyle modification, supported with pharmacotherapy of obesity, can make a substantial difference in most musculoskeletal symptoms.

Through this review we attempt to provide a concise but comprehensive resource for approaching the rheumatological aspects of obesity, and provide guidance on how to manage patients who are comorbid for some musculoskeletal diseases and obesity.

## Method

We searched PubMed (Medline) for English and Polish language articles on the associations between musculoskeletal disorders and obesity, using the search terms “musculoskeletal disorders”, “osteoporosis”, “osteoarthritis”, “back pain”, “fibromyalgia”, “rheumatoid arthritis”, “systemic lupus erythematosus”, “obesity”, and “overweight”. We tried to extract clinical and pro-

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spective cohort studies of sufficient size reporting well documented data. We reviewed these publications and relevant references in these papers and formulated our conclusions.

## Results

### Definition and diagnosis of overweight and obesity

According to the definition of the World Health Organization, overweight and obesity are considered as abnormal or excessive fat accumulation that presents a risk to health [1].

Scientific societies consistently describe obesity as a chronic disease characterized by excessive accumulation of body fat, increasing the risk of many metabolic disturbances and secondary disorders, including cardiovascular and neoplastic diseases [4].

Due to the location of excess body fat, gynoid (iliogluteal) and abdominal (central, visceral) types of obesity are distinguished. Especially the latter leads to the development of insulin resistance and further metabolic disturbances – glucose intolerance, dyslipidemia, as well as many diseases, including T2DM, asthma, chronic obstructive pulmonary disease, sleep apnea syndrome, hypertension and other cardiovascular diseases, gastroesophageal reflux, non-alcoholic fatty liver, various types of cancers, hypogonadism, polycystic ovary syndrome, infertility, depression, and musculoskeletal disorders [5].

Obesity diagnosis is based on the assessment BMI, which is calculated by dividing the body weight (in kg) by the square of height (in m). The normal BMI is 18.5–24.9 kg/m<sup>2</sup>. Values from 25.0 to 29.9 kg/m<sup>2</sup> indicate overweight (pre-obesity state), from 30.0 to 34.9 kg/m<sup>2</sup> obesity class I, from 35.0 to 39.9 kg/m<sup>2</sup> obesity class II, and values from 40.0 kg/m<sup>2</sup> indicate obesity class III (severe, morbid).

In everyday practice additional measurement of the abdomen circumference is highly recommended. For men, a waist circumference below 94 cm is “low risk”, 94–102 cm is “high risk” and more than 102 cm is “very high”. For women, values of low, high and very high risk are 80 cm, 80–88 cm and more than 88 cm, respectively. These are the guidelines for people of white European, black African, Middle Eastern and mixed origin [6].

According to a new definition of metabolic syndrome proposed in 2020 by nine Polish scientific societies, waist circumference from 88 cm in women and 104 cm in men is an essential criterion in diagnosis of this syndrome [7].

## Epidemiology

The WHO estimates that 1 billion people worldwide are obese – 650 million adults, 340 million adolescents and 39 million children. This number is still increasing. The WHO anticipates that by 2025, approximately 167 million people – adults and children – will become less healthy because their body weight is too high [1].

In Poland in 2020 54% of inhabitants were overweight, more often men (64%) than women (46%). The prevalence of obesity (BMI  $\geq$  30) was estimated at 10% (12% among men and 8% among women). Excessive body weight among school-aged children and youth aged 11–16 has risen in recent years (more in boys than in girls) to 16.5%. During the COVID-19 pandemic period, between spring and autumn 2020, 28% of Poles aged 20 or older (28% of men 29% of women) reported an increase in their body weight [2].

## Etiology

Obesity in most cases is of primary nature. It means, that it develops under the influence of environmental factors that overlap the underlying genetic background. More than 400 genes that may be involved in excessive accumulation of fat have been described. Among the environmental factors associated with the over-abundant fat gain the reduction of physical activity and hypercaloric diet with meals rich in saturated fats, cholesterol, and simple carbohydrates, but poor in polyunsaturated fatty acids and fiber are considered to be the most important.

A major role is attributed to proper nutrition during fetal life. Among newborns with low birth weight, childhood obesity and cardiovascular diseases later in adulthood are significantly more common [8]. Also, an association between high levels of birth weight and increased odds of obesity among older children and adolescences was found [9].

Secondary obesity may be the result of endocrine disorders (hypercortisolemia, hypothyroidism, hypogonadism, growth hormone deficiency), the effects of certain drugs (phenothiazine derivatives, H1-receptor antagonists, oral contraceptives, antidepressants, antiepileptic drugs, antidiabetic drugs, glucocorticosteroids,  $\beta$ -blockers) and less often other causes [10].

## Obesity and the musculoskeletal system

Disorders and diseases of the musculoskeletal system that could be affected by obesity include:

- osteoarthritis,
- back pain,
- low bone mass (osteopenia, osteoporosis),

- diffuse idiopathic skeletal hyperostosis (Forestier's disease),
- postural instability,
- soft tissue diseases (e.g. carpal tunnel syndrome, plantar fasciitis),
- gout,
- fibromyalgia,
- connective tissue diseases (rheumatoid arthritis, systemic lupus erythematosus and others) [11].

Osteoarthritis is the most common skeletal disease. Numerous epidemiological studies indicate that there is a clear relationship between BMI and the severity of degenerative changes, assessed both clinically and by X-ray examination [12, 13]. Also studies with magnetic resonance imaging (MRI) have shown a correlation between body weight and the degree of articular cartilage damage [14]. It has been calculated that the odds ratio (OR) for the development of degenerative knees changes with an increase in BMI by 5 units is 1.6 [15]. Studies of twins have shown that already an increase in body weight by 1 kg increases the risk of radiological changes in the knee and metacarpal joints [16].

The influence of obesity on the development of osteoarthritis involves the participation of many factors, both of mechanical and metabolic nature. Joints, especially weight-bearing (hip and knee) are constantly subjected to mild damage through motions. It causes a state of persistent wound healing and repair processes. As a result, the articular cartilage and neighboring bone must continually rebuild where synthesis and degradation are a constant process [17].

This mechanical effects of obesity on joints may depend on the arrangement of bone structures. For example, the clawed position of the femurs intensifies the effect of excessive body weight on the knee joints, while in the valgus setting, obesity is not so important [18]. The element of movement should also be taken into account. Under physiological conditions, the pressure on the cartilage of the knee joints during walking increases about three times. When running or climbing stairs, this pressure increases 6–10 times. It is clear that in the case of obesity, such burdens must be particularly destructive [19].

While the mechanical component was believed to be the main cause of osteoarthritis recent studies have proven that other factors such as adipose deposition, insulin resistance, and especially the improper coordination of innate and adaptive immune responses may lead to the initiation and progression of obesity-associated destruction of the joints. Multi-type inflammatory cells, especially macrophages that produces pro-inflammatory cytokines are recruited into the synovial fluid and play important role in pathological changes in the joints.

Higher leptin levels both in serum [20] and synovial fluid [21] in severe osteoarthritis have been found. Also, a relationship has been identified between the levels of this adipokine and the severity of joint lesions, including cartilage damage [22]. Likewise, it has been demonstrated, that an important role is played by chronic subclinical inflammation caused by increased activity of other cytokines: tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) or interleukin-6 (IL-6) [23]. Levels of these proteins are proportional to the severity of pain. Moreover, the higher they are, the less effective is the analgesic treatment [24].

Other cells – neutrophils, eosinophils, and dendritic cells are also involved in the pathogenesis of osteoarthritis, although their function has not been fully resolved. The interplay between a variety of immune cells and other cells that reside in the articular joints may constitute a vicious cycle, leading to pathological changes of the articular joint in obese individuals [25].

Another common health problem is back pain. Excessive body weight appears to promote greater exposure to radicular pain and neurological symptoms. Particularly, chronic pain seems to be associated with an increase in BMI [26, 27]. Research using MRI in a group of physically working middle-aged men showed that overweight/obesity is associated with a decrease in the signal from the intervertebral discs, although it has not been established to what extent this affects clinical symptomatology [28].

There are several potential mechanisms of the relationship between excess body weight and back pain. Obesity may increase the mechanical load on the spine by causing a higher compression on the lumbar spine structures. Individuals with high body weight are more predisposed to injuries [29]. Moreover, systemic inflammation and pathomechanical pathways associated with obesity may play a role in etiology of back pain [30].

A recent systematic review of twin studies revealed that overweight or obese individuals are more likely to have low back pain and lumbar disc generation, but the associations were weaker after controlling for familial factors, suggesting that obesity and low back pain share common genetic risk factors [31]. In obese patients, the possibility of adipose tissue expansion within the dura mater, which may narrow the lumen of the spinal canal has also been found [32].

Numerous observations indicate the relationship between BMI and bone mass. It has even been calculated that an increase in body weight by 10 kg is associated with an increase in bone mineral density (BMD) by 1% [33]. This is, in part, the result of more intense androgen aromatization in a greater amount of adipose tissue with a subsequent increase in levels of estrogen – hormones that are crucial for maintaining bone mass.

A mechanical effect – increase of the pressure forces on the bone in conditions of greater body weight also comes into play. Apoptosis of osteoblasts is then inhibited, while the proliferation and differentiation of these cells and of osteocytes are stimulated due to activation of the Wnt/ $\beta$ -catenin system as well as to inhibition of PPAR $\gamma$  receptor expression [34].

Moreover, it is believed that there is a close relationship between regulation of the whole body's energy balance and bone homeostasis in the central nervous system (CNS). Such integration may function owing to many mediators, including leptin and adiponectin of adipose tissue origin. Also, proinflammatory cytokines released from this tissue that is altered in obesity, such as TNF- $\alpha$ , interleukin-1 (IL-1) or IL-6 are important mediators of osteoclast differentiation and bone resorption.

The adverse effects of a high-fat diet on the absorption of calcium from the gastrointestinal tract should also be taken into consideration. This is all the more important because hypovitaminosis D is usually found in obesity, what worsening the absorption of substrates necessary for bone formation from the gastrointestinal tract.

There is evidence to suggest that the relationship between body weight and bone mass is in fact bidirectional: not only does the former determine the latter, but bone mass may also be one of the factors influencing body weight [35]. The mechanism of this phenomenon has not been fully resolved, but the participation of osteocytes is suspected. It is suggested, that these cells may react not only in short-term mode to changes in pressure on the bone in the mechanism of the mechanostat, but also in the long-term mode affect the absorption of energy by the body depending on bone mass [36].

Although obesity was previously thought to protect against osteoporosis and fractures, it is currently known that the problem is of a much more complex nature. The protective role of high body weight may be related to greater muscle mass rather than to gain of fat mass, which in fact is a factor accelerating the decline of BMD. Moreover, the type of obesity is important – excess fat in the abdominal cavity is particularly unfavorable, while subcutaneously located fat depots do not adversely affect bone mass [37].

In general, the bone of obese people is more prone to fractures compared to their lean counterparts. The reasons are the increased fat mass in the bone marrow, which accumulates during bone formation, as well as higher levels of proinflammatory cytokines released from fat tissue, that activate osteoclasts responsible for bone resorption. *FTO* gene mutations and accelerated aging of osteoblasts, responsible for bone synthe-

sis are also play important role [36]. These findings are confirmed by epidemiological studies, e.g. observation of a group of older men (Osteoporotic Fractures in Men Study) showed that an increase in BMI did not protect against bone fractures [38].

It is also well known that patients with T2DM, usually overweight or obese, are more inclined to bone fractures, despite normal or even higher BMD compared to healthy controls [39]. The higher incidence of fractures also results from the enhanced tendency to falls among obese and especially elderly (> 60 years of age) persons.

There are many reasons for this effect. One of them is the most frequent occurrence of serious diseases, such as T2DM, cardiovascular diseases, arthritis, sleep apnea syndrome and others leading to a general deterioration of health. These diseases, especially diabetes, lead to further complications such as peripheral neuropathy, disruption of autonomic nervous system function or orthostatic hypotension, contributing to instability. Excessive body weight makes it difficult to perform everyday activities – climbing stairs, washing, etc., which further increases the risk of falls. Finally, obesity changes the statics of the whole body (increase in pressure on the heel part of the foot), again leading to poor balance [37]. A higher waist-to-hip ratio is an independent factor of instability, at least in women [40].

Much less common than back pain or low bone mass is diffuse idiopathic skeletal hyperostosis. Forestier's disease is characterized by bone growth in places of tendon attachments, aponeuroses, and joint capsules. The lesions are particularly strongly expressed within the thoracic vertebrae, where alleged large osteophytes resembling parrot beaks, usually involving several vertebrae can be seen. Changes are also found within the inner lamina of the frontal bone. Although the etiology of the disease is not well understood, it has been shown to be more common in people with a high BMI [41]. Leptin levels in patients with spontaneous hyperostosis are higher than in the general population [42].

The impact of obesity on the movement mechanics is unfavorable. Excessive body weight causes flattening of the natural arches of the feet. As a result, excessive movement of the hindfoot is marked during walking, which leads to excessive abduction of the front part of the foot. There is also an overload of the joints of the foot. The whole posture changes – it becomes less stable, with excessive deviations of the trunk [43]. Severe obesity additionally slows down movement, and significantly shortens the distance of walking.

Obesity also adversely affects the structure and functions of soft tissues that are the part of the musculoskeletal system. Excessive body weight has been

shown to increase the risk of tendonitis associated with work in the upper limbs [44]. High BMI contributes to the development of carpal tunnel syndrome – the odds ratio (OR) in such cases is 2.06 [45]. Also, the higher incidence of plantar fasciitis is associated with obesity. In these cases OR of unilateral inflammation increases to 5.6 compared to persons with normal BMI [46].

Excessive body weight is one of the recognized factors in the etiology of gout. A direct relationship between serum uric acid levels and BMI has been found [47]. The clearance of uric acid in obesity is reduced.

Fibromyalgia is a disorder characterized by widespread musculoskeletal pain accompanied by fatigue, sleepiness, memory and mood issues. It is believed, that fibromyalgia amplifies painful sensations by affecting the way that brain and spinal cord process painful and nonpainful signals. Although the etiology of this disease is not fully understood and probably is complex obesity is considered as a one of the factors contributing to its development [48].

The most common systemic connective tissue disease is rheumatoid arthritis (RA). It has been evidenced, that one of the risk factors of this severe disease is BMI > 30, and that excessive body weight worsens the patients quality of life. The role of obesity in RA etiology is not clear, but the elevated secretion of adipokines (leptin, visfatin, adiponectin) suggests their role in the mechanism of chronic inflammation, which is the crucial process in the course of this disease [49].

A recent meta-analysis showed that people with obesity tend to have higher disease activity scores and lower response rates for both traditional disease-modifying antirheumatic medications and biological drugs [50].

Obesity could also affect the course of systemic lupus erythematosus (SLE). Studies have reported a high predominance of obesity in SLE in the range 29–50%. Increase in fat mass through the release of pro-inflammatory cytokines could modify the severity of this disease and contributes to increased cardiovascular risk. Actually, reports have noted that obese SLE patients have increased gene and protein expression of various pro-inflammatory cytokines such as interleukin-23 (IL-23) and TNF- $\alpha$  [51].

In fact, obesity is a state of chronic low-grade inflammation, associated with altered immune function and the release of several different adipokines; e.g. elevated levels of leptin have been detected in SLE patients and it is believed that this adipokine could be the connection between obesity and SLE [52, 53].

Obesity contributes to the progressive disability of patients with the musculoskeletal system disorders. Persons with disabilities are 2.5 times more likely to be obese than their healthy counterparts [54]. Weight loss

in such cases usually leads to increased mobility and to decrease in the perception of pain by sufferers.

### **Management of obesity – effects on musculoskeletal disorders**

The epidemic nature of obesity and the serious health consequences that it causes (only those related to the musculoskeletal system are included in the study) require an concerted and multipronged approach in the management of this disease.

Many publications show the beneficial effects of weight reduction in the musculoskeletal system, e.g. loss of at least 10% of body weight, coupled with exercise, is recognized as a keystone in the management of obese patients with osteoarthritis, and can lead to significant improvement in symptoms, pain relief, physical function and health-related quality of life.

Some evidence supports in these cases a low-calorie diet, although it should be kept in mind that such a diet, especially in the elderly, must provide all the essential nutrients and recommended daily calcium to reduce the risk of osteoporosis. In some patients, compliance with long-term life-style modification is poor and other approaches, such as pharmacotherapy or bariatric surgery, may be a better way to achieve weight loss [55]. It was reported recently that a weight loss > 7.5% is required to reduce the risk of total knee replacement in adults with overweight or obesity [56].

In the case of back pain it has been reported that pain in the cervical and lumbar spine, as well as foot pain, may disappear after significant weight reduction, e.g. as a result of lifestyle modification or bariatric surgery [57]. However, there is a lack of high-quality trials on the effect of various weight loss programs focused on individuals with low back pain. In fact, there is very low-quality evidence on this topic, although compliance is an important barrier to implementation of weight loss programs [58].

Also, the limited quantity of scientific data rules out drawing strong conclusions about the benefit of weight loss in obese patients with fibromyalgia. However, it was observed that weight reduction, e.g. as a result of lifestyle modification or bariatric surgery, led to reduced pain perception, clinical improvement, and better quality of life [48]. In another study a significant decrease in median pain scores (from 9 to 3) in patients with fibromyalgia was found after bariatric surgery [59].

Although obesity is very common in patients with inflammatory rheumatic diseases (IRDs), of which between 27% and 37% of patients have a body mass index  $\geq 30$  kg/m<sup>2</sup> only a few trials have evaluated the effect of weight loss on arthritis activity.

One recently published study showed that in patients with rheumatoid arthritis or psoriatic arthritis with a substantial weight loss of > 10% of body mass, median Disease Activity Score 28 joints score decreased by 0.9. This reduction in disease activity resulted in an increase in the percentage of patients achieving remission from 6% to 63%. This reduction in disease activity was obtained without intensification of medical treatment in 87% of the patients. This case series supports the current evidence that weight reduction has positive effects on the course of the disease and thus can serve as a non-pharmacological treatment option in obese patients with inflammatory rheumatic diseases [60].

The therapy of obesity always should be individualized, although a reasonable goal may be reducing the body weight by 5–15% within 6 months with its subsequent maintenance and trying to reduce it further. Physician efforts should not be limited to BMI control, but should also consider other health risk factors: blood pressure, fasting and post-meal glucose, blood lipids, the degree of disability and finally the quality of life. Detailed methods of treatment are specified in the scientific societies guidelines (in our country the Polish Society for the Study on Obesity [PTBO], the Polish Society for the Treatment of Obesity [PTLO] and others).

In general, treatment includes three ways of action:

1. Lifestyle modification – changing eating habits, especially reducing the amount of calories consumed daily (recommended minus 600–700/day in relation to individual energy needs) and increasing physical activity.

2. Indications for starting on with pharmacotherapy are: BMI exceeding 30 kg/m<sup>2</sup> or BMI > 27 kg/m<sup>2</sup>, when is accompanied by at least one of the complications of obesity (e.g. type 2 diabetes, sleep apnea, osteoarthritis). Pharmacotherapy must be an addition to lifestyle modification when such a procedure is not sufficiently effective. Drugs approved in the European Union and in Poland for the treatment of obesity are liraglutide, semaglutide, naltrexone with bupropion and orlistat. Detailed rules for the use of each drug are specified in the guidelines of the scientific societies and in the characteristics of medical products.

3. Surgical treatment. It is the most effective method of treating obesity. It should not be precluded, as it causes a long-term reduction in body weight by 20–40% and improvement in terms of accompanying disturbances and diseases. The indications are severe obesity, i.e. BMI > 40 kg/m<sup>2</sup> or obesity with BMI > 35 kg/m<sup>2</sup>, when it is accompanied by complications and medical treatment is ineffective. People between 18 and 60 years of age may be candidates for surgery. Excess weight loss induced by bariatric surgery seems to produce significant and clinically

relevant effects in decreasing pain in patients with knee osteoarthritis or chronic lumbago, although these findings require further confirmation in prospective controlled trials. Also, rheumatoid arthritis outcomes appear to improve following bariatric procedures. On the other hand, this method of treatment may have deleterious effects on bone metabolism, and there is a considerable body of evidence showing that this can lead to an increase in fracture risk, particularly in patients operated on with malabsorptive techniques [61].

## Conclusions

Obesity is now considered as a chronic disease that is the real “tsunami of the twenty-first century”. The musculoskeletal system diseases are the first cause of disability and are the second most common cause of visits to primary care physicians. As has been shown in many epidemiological and observational studies, excessive body weight is an important risk factor for the onset and worsening of many musculoskeletal diseases. The mechanisms underlying relationships between BMI and these disorders are complex and in many cases are still waiting to be fully explained.

Obesity, due to its epidemic nature and the serious health problems it brings about requires energetic treatment, based on lifestyle modification, supplemented, if necessary, by pharmacological, and in justified cases surgical treatment.

There is now a lot of scientific evidence on the beneficial effects of weight reduction in the musculoskeletal system.

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