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Obesity impact on bones and joints health

Abstract

Introduction and objective

Obesity, characterized by excessive fat accumulation, poses significant health risks. The WHO classifies overweight as a BMI of 25 to <30 kg/m² and obesity as a BMI of ≥30 kg/m², divided into three classes. This study examines the relationship between obesity and bone health, focusing on osteoarthritis (OA), rheumatoid arthritis (RA), and fracture risks.

Review methods

A review of epidemiological and clinical studies was conducted, including WHO statistics, U.S. obesity trends, and recent findings on the mechanisms linking obesity with bone health and joint diseases. Studies were selected for their relevance to understanding obesity's impact on skeletal health.

Abbreviated description of the state of knowledge

Obesity is influenced by sociodemographic, behavioral, and genetic factors. While excess weight was once considered beneficial for bones due to increased mechanical loading, recent research shows its harmful effects. Obesity is linked to chronic inflammation, altered adipokine levels, and higher risk of atypical fractures. In OA, obesity accelerates joint degeneration through mechanical and metabolic pathways. In RA, obesity is associated with increased disease activity and cardiovascular complications.

Summary

Obesity significantly affects bone and joint health, increasing the risk of OA, RA, and fractures. The paradox of obesity providing mechanical benefits while causing metabolic and inflammatory issues is crucial. Understanding these mechanisms is vital for developing effective prevention and management strategies for obesity-related skeletal diseases. Further research is essential to clarify the complex interactions between adipose tissue and bone health, aiming to improve outcomes for obese individuals.

Obesity:

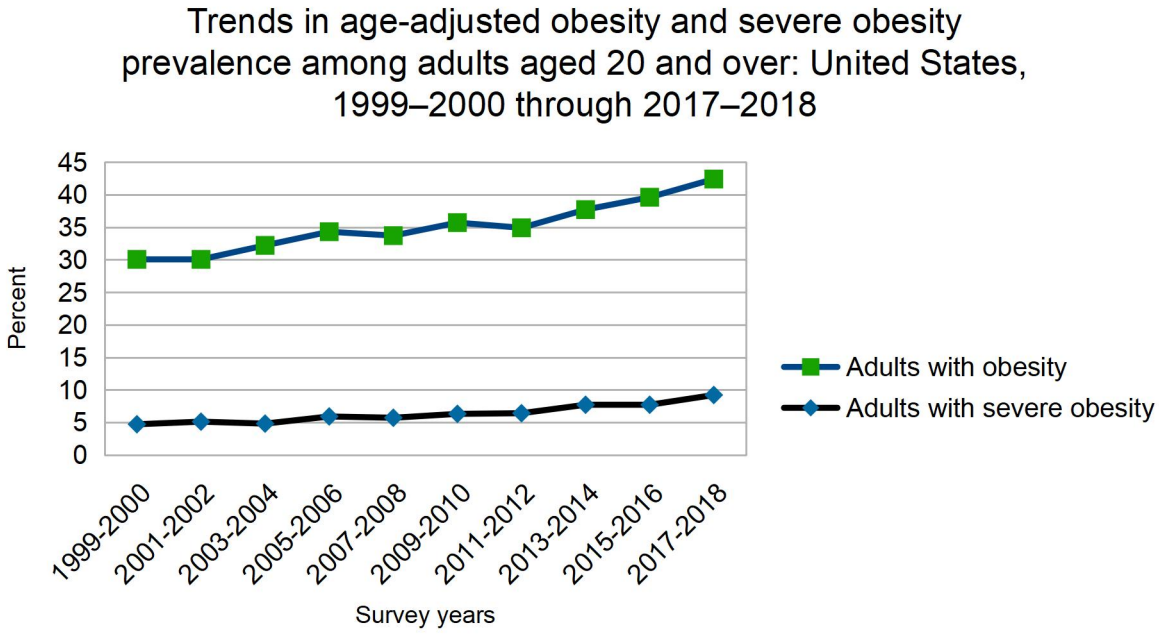
Excessive body weight and obesity are identified as pathological or excessive accumulation of adipose tissue, which can lead to health disorders. The Body Mass Index (BMI) is a simple ratio of height to weight, often used to distinguish between overweight and obesity in adults. The World Health Organization (WHO) defines overweight as a BMI value in the range of 25 to <30 kg/m², while obesity is defined as a BMI value of ≥30 kg/m². Additionally, obesity can be categorized into three degrees: Class I obesity (30 to <35 kg/m²), Class II obesity (35 to <40 kg/m²), and Class III obesity (≥40 kg/m²) [2].

Table 1: BMI Values for Adults and Their Classification:

BMI Range	**Classification**
18.5 to 24.9	Healthy weight
25 to 29.9	Overweight
30+	Obesity
40+	Extreme obesity

According to official statistics presented by the WHO, in 2022, 2.5 billion adults aged 18 and older were overweight, including over 890 million adults suffering from obesity. This accounted for 43% of all adults aged 18 and older (43% of men and 44% of women) being overweight. This is an increase compared to 1990 when 25% of adults aged 18 and older were classified as overweight [3].

Epidemiological studies conducted in the United States in 1990, 2000, 2010, and 2020 observed a significant increase in the percentage of individuals affected by obesity within the population. In 1990, the percentage of obese individuals was approximately 15%, which increased to 25% in 2000. By 2010, this percentage had reached 35%, and the latest data from 2020 show an even further increase, exceeding 40%. This continuous upward trend in obesity within the United States population represents a significant challenge for healthcare systems and necessitates effective preventive measures [12][13][14].



Obesity is a complex health issue, the occurrence of which is determined by a range of sociodemographic, behavioral, and genetic factors. In the context of sociodemographic factors, age, marital status, wealth index, and place of residence show significant associations with the risk of obesity. The increase in urbanization and changes in food consumption patterns and availability can also contribute to the rise of this condition. Behavioral factors such as unhealthy eating habits, lack of physical activity, excessive alcohol consumption, and prolonged screen time are also significant risk factors. Additionally, there is a strong link between genetics and obesity, where a family history of obesity and certain genetic predispositions, such as the presence of the FTO gene, can increase susceptibility to developing this condition. Understanding and considering these diverse factors are crucial for the effective prevention and management of obesity [6][7][8][9][10][11].

Impact of Obesity on Bone Health:

Previous studies have focused on analyzing the relationships between obesity and the skeletal system; however, the results obtained are inconclusive. Despite obesity being a health risk factor, it was previously considered beneficial for bone health due to the positive effect of mechanical loading exerted by high body weight on the bone formation process. However, other studies on this topic have not reached a clear consensus, instead suggesting that excessive fat mass resulting from obesity may not protect against osteoporosis and may actually be harmful to bones, potentially causing osteoporosis. Since both adipocytes and osteoblasts are derived from a common multipotent mesenchymal stem cell, obesity may increase adipocyte differentiation and fat accumulation while simultaneously decreasing osteoblast differentiation and bone formation [45][46][47].

Obesity and Bone Inflammation:

Obesity is associated with a chronic inflammatory state resulting from increased circulation and tissue presence of pro-inflammatory cytokines. These cytokines can stimulate osteoclast activity and lead to bone resorption through modifications in the signaling pathway related to the receptor activator of NF-κB (RANK)/RANK ligand/osteoprotegerin. Additionally, excessive production of leptin and/or reduced expression of adiponectin by adipocytes in obesity can directly affect the bone formation process or indirectly influence bone resorption through increased production of pro-inflammatory cytokines [1][2][4][5].

Bone Fractures in Obese Individuals:

Obesity, despite its protective effect on certain fracture locations such as the hip, spine, and wrist, paradoxically increases the risk of fractures in other, less typical sites. This phenomenon, known as the "obesity fracture site paradox," highlights that higher body mass protects against osteoporotic fractures in some locations but simultaneously increases the risk of fractures in areas such as the ankle, upper leg, and arm. Studies show that fall mechanisms and the anatomy and physiology of obese individuals play a key role in this phenomenon. For example, the abundant fat accumulation around the hips may protect against hip fractures, while the lower fat protection in the lower and upper limbs may increase the risk of fractures in these areas. Additionally, the manner of falls in obese individuals and their tendency toward excessive ankle joint movements may contribute to a higher risk of injuries.

The increased risk of falls in obese individuals is well-documented in the literature. Factors such as reduced agility, greater postural instability, limited physical activity, dynapenic obesity, and the presence of comorbidities (e.g., diabetes, cardiovascular diseases, obstructive sleep apnea) contribute to this risk. These factors lead to balance and coordination disorders, increasing the likelihood of falls and fractures [15][17][18][19][20][21].

Table 2: Factors Increasing Fall Risk in Obese Individuals

Risk Factors	**Description**
Excessive body weight	Reduced agility and slowed reaction time during falls
Postural instability	Lower body stability, especially in older women with central adiposity
Limited physical activity	Lower muscle strength and agility due to reduced daily exercise
Dynapenic obesity	Lower muscle strength due to fatty infiltration in muscles
Comorbid conditions	Diabetes, cardiovascular diseases, sleep apnea, leading to peripheral neuropathy, orthostatic hypotension, and general weakness

Table 3: "Obese's Fracture Site Paradox"

Fracture Site	Risk in Obese Individuals	Protective/Risk Mechanisms
Hip	Lower risk	Abundant fat padding around hips providing cushioning
Spine	Lower risk	Better protection by fat
Wrist	Lower risk	Lower impact force on wrist
Ankle	Higher risk	Tendency to excessive ankle movements, minimal fat protection
Upper leg	Higher risk	Increased fall risk, minimal fat protection
Humerus (arm)	Higher risk	Increased fall risk, minimal fat protection

Pathomechanism of Osteoarthritis (OA)

Osteoarthritis (OA) is the most common degenerative joint disease in older adults, particularly affecting the knee joint. OA is characterized by the gradual degeneration of articular cartilage and structural changes in the entire synovial joints, including the synovial membrane, meniscus, fat tissue, periarticular ligaments, and subchondral bone. Clinical and experimental studies have shown that age-related OA is the result of multiple factors, including age, sex, injuries, and obesity. Among these factors, obesity is one of the most significant and modifiable risk factors [16][22][23][24][25].

The Relationship Between Obesity and Joint Inflammation

There is growing evidence indicating a strong association between obesity and inflammation. Adipose tissue plays a role in regulating inflammatory immune responses in cartilage. Individuals and animals affected by obesity exhibit higher serum levels of TNF-α, IL-1, and IL-6, which are produced by macrophages in adipose tissue. Concurrently, levels of TNF-α, IL-1, and IL-6 in synovial fluid, synovial membrane, subchondral bone, and cartilage in patients with OA are elevated, confirming their significant role in the pathogenesis of OA. TNF-α, IL-1, and IL-6 are cytokines produced by adipose tissue that directly and negatively affect cartilage. Furthermore, TNF-α, IL-1, and IL-6 can promote the production of other factors such as matrix metalloproteinases (MMPs) and prostaglandins, while inhibiting the synthesis of proteoglycans and type II collagen. Thus, they play a key role in the degradation of OA cartilage matrix and bone resorption. Additionally, TNF-α, IL-1, and IL-6 can indirectly cause OA by regulating adiponectin and leptin secreted by fat cells [26][27][28][29].

Impact of Obesity on the Risk of OA

Overweight or obesity increases the risk of OA in all three joint areas (knees, hips, and hands), particularly in the knees. Overweight, Class I obesity, and Class II obesity increased the risk of knee OA by 2-fold, 3.1-fold, and 4.7-fold, respectively [30].

The Role of Adipokines in the Pathogenesis of OA

Adipokines are a new class of compounds now considered key molecules involved in the pathogenesis of rheumatic diseases. Resistin is an adipokine closely associated with obesity, local inflammation, and metabolic syndrome. Recent studies have shown that serum levels of resistin were higher in patients with primary knee arthritis than in healthy controls. Additionally, elevated serum resistin levels were positively correlated with obesity indices, inflammatory markers, and the WOMAC index (a measure of OA symptom severity). Moreover, the combination of leptin and IL-1 can promote the production of MMP-1, MMP-3, and MMP-13 in human OA cartilage. The effect of leptin on MMP-1, MMP-3, and MMP-13 was mediated by the transcription factor NF-κB and the protein kinase C and MAP kinase pathways. Leptin concentration in synovial fluid was also positively correlated with levels of MMP-1 and MMP-3 in patients with OA. These findings demonstrate that leptin has a catabolic effect on OA joints by increasing the production of MMPs in cartilage [31][32][33][34][35][41].

The Role of Adiponectin in the Pathological Process of OA

Adiponectin has also been reported to be involved in the pathophysiological process of osteoarthritis (OA). Studies have shown that the total amount of nitric oxide (NO) and levels of MMP-1, MMP-3, and MMP-13 were increased in adiponectin-stimulated OA chondrocytes compared to unstimulated cells. NO is one of the main mediators of the pro-inflammatory cytokine effects on chondrocytes and also regulates various cartilage functions, including chondrocyte phenotype loss, apoptosis, and extracellular matrix degradation. In the study, adiponectin increased the expression of MMPs and iNOS in human OA chondrocytes through the AMPK and JNK pathways, leading to the degradation of the OA cartilage matrix [36][37][41].

In summary, obesity not only increases the prevalence of OA, especially in weight-bearing joints such as the knees, but is also associated with non-weight-bearing joints such as the fingers and wrists, suggesting that these metabolic mediators contribute to the increased incidence of OA in obese individuals. This may be because obesity increases the mechanical load on articular cartilage, leading to its degradation, and adipose tissue secretes metabolic factors (such as IL-1, TNF-α, adiponectin, and leptin), leading to a higher prevalence of OA in obese individuals [38][39][40][41].

Chart: Increase in the Risk of Knee OA Based on the Degree of Obesity

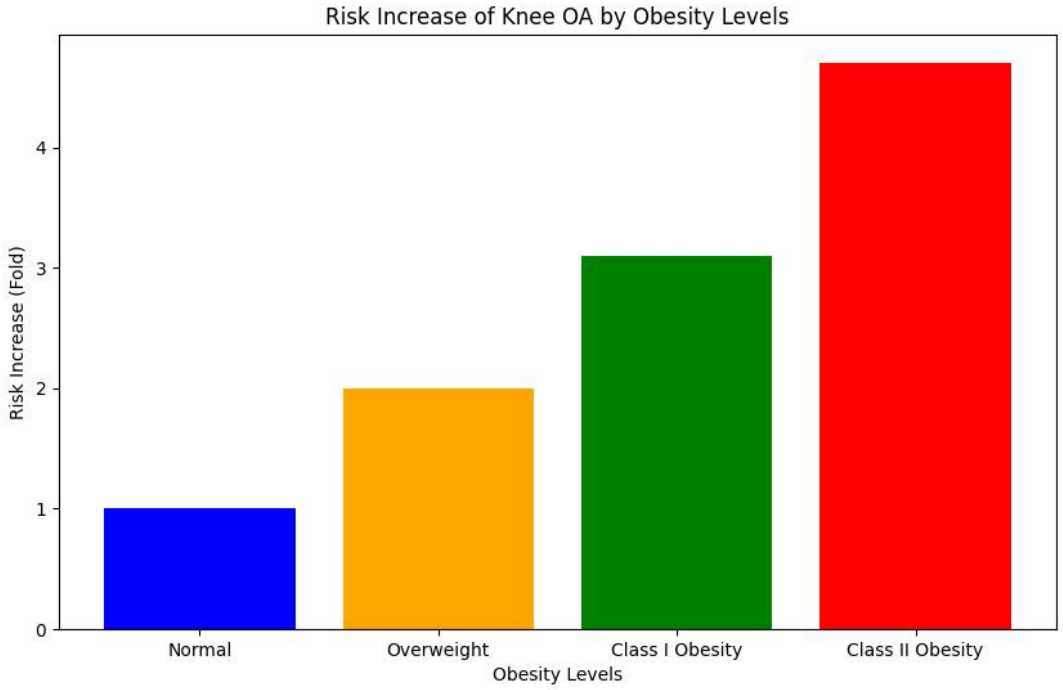


Chart Description:
The chart illustrates the increase in the risk of knee osteoarthritis (OA) based on the degree of obesity. The relative risk of knee OA is twice as high in individuals who are overweight, 3.1 times higher in individuals with Class I obesity, and 4.7 times higher in individuals with Class II obesity compared to those with normal body weight [30].

The Impact of Obesity on the Course of Rheumatoid Arthritis (RA)
The association between obesity and RA is highly significant due to its effects on both symptom severity and the risk of cardiovascular complications. A study by Katrien Van Raemdonck and other authors [44] examines this issue, focusing on the relationship between overweight and disease activity as well as inflammatory markers in RA patients. In an analysis combining a cohort of chronically ill RA patients, it was shown that obesity directly influences the severity of joint symptoms, particularly in the lower extremities. RA patients with excess body weight tend to have a greater number of swollen joints in the lower extremities, which may affect the accuracy of disease activity assessment, especially when using classical measures such as DAS28, which do not include assessment of the lower extremities. Additionally, the study indicates an increased risk of cardiovascular complications in RA patients with obesity, confirming the need for monitoring this patient group considering both disease activity and cardiovascular prophylaxis.
In a study conducted by Veena K. Ranganath and colleagues [43], an analysis was performed on the impact of obesity on the activity of rheumatoid arthritis (RA), with particular emphasis on the clinical assessment of joint swelling. Based on a cross-sectional cohort of 323 patients

with early RA, the relationship between body mass index and disease activity measures, including the number of swollen joints, was evaluated.

The results indicate a direct relationship between obesity and increased swelling of the lower limb joints in RA patients. Higher disease activity scores based on DAS44 were observed in obese patients, mainly due to the increased number of swollen lower limb joints. High scores of joint swelling assessment in the lower limbs in obese patients may be related to excessive periarticular adiposity or other factors.

In a study published by M. Changulani and colleagues [42], the relationship between body mass index (BMI) and the age of patients undergoing hip or knee joint replacement surgery was examined. The study included 1369 patients, of whom 1025 underwent hip joint replacement and 344 knee joint replacement. Patients were divided into five groups based on their BMI.

Table 4: Mean Age of Surgery by BMI Group

BMI Group	**Number of Patients**	**Mean Age of Surgery (years)**
Normal (< 25)	281	71
Overweight (25-29.9)	491	68
Moderately Obese (30-34.9)	163	69
Severely Obese (35-39.9)	67	65
Clinically Obese (≥ 40)	23	61

The Impact of Obesity on the Progression of Rheumatoid Arthritis (RA)

The relationship between obesity and RA is highly significant due to its effects on both symptom exacerbation and the risk of cardiovascular complications. A study conducted by Katrien Van Raemdonck [44] and other authors examines this matter, focusing on the correlation between overweight and disease activity as well as inflammatory indicators in RA patients. In an analysis encompassing a cohort of chronically ill RA patients, it was demonstrated that obesity directly influences the severity of joint symptoms, particularly within the lower extremities. RA patients with excess body weight tend to exhibit a greater number of swollen lower limb joints, which may impact the accuracy of disease activity assessment, especially when utilizing conventional measures such as DAS28 that do not encompass lower limb evaluation. Additionally, the study suggests an elevated risk of cardiovascular complications in RA patients with obesity, emphasizing the necessity for monitoring this patient subgroup considering both disease activity and cardiovascular preventive measures.

In a study conducted by Veena K. Ranganath and colleagues [43], an analysis was carried out on the impact of obesity on rheumatoid arthritis (RA) activity, with a particular focus on the clinical evaluation of joint swelling. Based on a cross-sectional cohort of 323 patients with early RA, the association between body mass index and disease activity metrics, including the quantity of swollen joints, was assessed. The findings indicate a direct correlation between obesity and increased lower limb joint swelling in RA patients. Elevated disease activity assessment scores based on DAS44 were observed in obese patients, primarily due to the

heightened number of swollen lower limb joints. The heightened assessment scores of joint swelling in the lower limbs in obese patients may be linked to excessive periarticular adiposity or other factors.

In a study published by M. Changulani and colleagues [42], the relationship between body mass index (BMI) and the age of patients undergoing hip or knee joint replacement surgery was investigated. The study comprised 1369 patients, among whom 1025 underwent hip joint replacement and 344 knee joint replacement. Patients were categorized into five BMI groups.

Conclusions

Obesity is a multifaceted health issue significantly impacting bone and joint health. The escalating prevalence of obesity worldwide, as indicated by WHO data, underscores the necessity for effective preventive and interventional measures. Despite previous assumptions that obesity may protect against osteoporosis, current research suggests that excess fat mass may be detrimental to bones, leading to structural weakening through cellular differentiation mechanisms and sustained inflammation. Pro-inflammatory cytokines produced in obesity may contribute to bone resorption, while mechanisms of falls and anatomical features of obese individuals increase the risk of fractures in atypical locations such as the ankle and shoulder.

Obesity also plays a pivotal role in the pathomechanism of osteoarthritis (OA). Obesity increases the risk of OA, particularly in the knee joints, through both mechanical loading and metabolic action of adipokines such as leptin and adiponectin. These metabolic factors may lead to cartilage degradation, as confirmed by elevated levels of pro-inflammatory cytokines and matrix metalloproteinases in joint tissue in individuals with OA.

The relationship between obesity and rheumatoid arthritis (RA) is equally significant. Obesity not only exacerbates RA symptoms, particularly in the lower limbs but also increases the risk of cardiovascular complications, underscoring the necessity for monitoring and appropriate treatment of RA patients with excess body weight.

Additionally, obesity influences earlier occurrence of hip and knee joint replacement surgeries. Patients with higher BMI tend to undergo these surgeries at a younger age, suggesting that obesity may accelerate joint degeneration.

In summary, obesity has a multifaceted impact on the musculoskeletal system, encompassing both mechanical and metabolic mechanisms of bone and joint damage. Effective obesity management and understanding its pathomechanisms are crucial for improving bone and joint health and the quality of life of individuals affected by this condition. Further research is necessary to better comprehend these relationships and develop appropriate therapeutic strategies.

Author's Contribution

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All authors have read and agreed with the published version of the manuscript.

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There are no conflicts of interests in the study

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