Assessment Of The Correlation Between Obesity And Fracture Risk: A Systematic Review With Meta-Analysis

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Abstract

Objectives: To evaluate the correlation between obesity and the risk of fractures by means of a systematic review with meta-analysis. Methodology: This is a systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology. Data collection took place between November 2023 and January 2024, with the last search date being January 31, 2023. Results: 13,263 participants were included, with an average age of 40 to 62 years. 02 studies reported the risk of ankle fractures in this population and another 02 evaluated the relationship by body segment. The main types of fracture related to obesity were ankle and lower limb fractures, most of which were associated with low-energy trauma. Conclusion: Ankle fractures were the main ones associated with obesity, while in areas such as the hip, the accumulation of surrounding fat can help dissipate energy after trauma, contributing to a reduction in fractures in these regions.

Keywords: Obesity; Fractures; Orthopaedic procedures.

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1. Introduction

Osteoporosis is defined as a reduction in bone mass, altering bone quality and increasing the propensity for fractures. The clinical presentation is diverse and previously followed the pattern of back pain, vertebral fractures, and osteopenia visualized by complementary plain radiography. With the evolution of the pathology, it is currently classified as a primary skeletal disorder causing metabolic changes that affect and compromise homeostasis throughout the body. There is an association between low bone mineral density and risk of fracture, a disease that has significant morbidity, mortality, and economic costs. [1]

Aging and/or estrogen deficiency is the predominant pathophysiological mechanism of bone mass loss leading to primary osteoporosis. However, other associated risk factors, such as frequent use of glucocorticoids in both sexes, contribute to a reduction in actual bone mineral density (BMD) and/or osteoporotic fractures. The prevalence is around 5 million men with diagnosed osteoporosis, due to insufficiency fractures, mainly due to: vertebral compression, wrist fractures, hip fractures, or fractures of the humerus/tibia. Recent studies indicate that in a COHORT of more than 5,000 men over 65 years of age, the main risk factor for increased fracture was obesity, and the ratio of women to men in hip fractures is approximately 2:1. 1,3,4,5,6

Physiopathologically, the pathology in question was once considered a disorder affecting older women in northern Europe, but it affects postmenopausal African Americans and is much more common in men than previously thought due to the use of glucocorticoids and/or immunosuppressive therapies for transplant patients. Therefore, it is currently a disease with multimodal involvement in both sexes, resulting in functional and homeostatic impairments.2,3,4

The diagnosis is made using various approaches: based on clinical presentation or through screening with periodic complementary tests. Dual-energy X-ray absorptiometry (DEXA) is a tool capable of predicting fractures in a large number of individuals by measuring BMD. For each standard deviation below the normal young adult average bone mineral density, there is an almost twofold increase in the risk of a subsequent hip fracture. Thus, qualitative measures of the skeleton, such as bone turnover, mineralization, and trabecular connectivity also contribute to the risk. 1.7 Furthermore, the pathology was rarely diagnosed before the widespread application of DEXA. In which, only in women with symptomatic vertebral fractures or osteopenia observed by radiography for other clinical reasons. Fact which, for a long time, hip fractures were dismissed as a consequence of aging or ignored in relation to treatment, resulting in drastic functional consequences. 7

The evolution of BMD by DEXA made it possible to evaluate a very strong predictor of future spine and hip fractures, since a single BMD measurement at any location can statistically enable the prevention of osteoporotic complications. Until the World Health Organization (WHO) established a cutoff point of 2.5 standard deviations below a normal young adult mean value for BMD in the spine or hip of postmenopausal women as an indicator of osteoporotic risk: epidemiological evaluation showed an increase in prevalence in women. In addition to effective therapeutic interventions. 7,8 Osteoporotic patients suffer fractures in the face of minimal trauma with low kinetic energy, marked by skeletal fragility and low bone mass. Therefore, the most significant risk factor for spinal, hip, or wrist fractures remains low BMD, which is confirmed using the FRAX score, which assesses: actual BMD plus clinical risk factors, including family history, BMI, smoking, and use of glucocorticoids. 7,8,9,10,11

The scientific relevance of the thematic discussion is based on the extent of low bone mass in relation to a lower frequency of osteoporosis diagnosis and low adherence to therapy. Approximately 70% of individuals who are at risk for osteoporosis and who are receiving therapy will not continue beyond the first year. 4 Thus, the objective of this study is to evaluate the correlation between obesity and the risk of fractures through a systematic review with meta-analysis. Contributing to the therapeutic approach and reduction of pathological complications in the affected population.

2. Methodology

A systematic review of the literature was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology. The research protocol was registered in the Systematic Reviews Protocol Registry (PROSPERO) under registration number CRD42024528338.

The selection of data from the literature was carried out between November 2023 and January 2024, with the last search date being January 31, 2023. Once the studies were identified, two independent reviewers performed the analysis.

Based on health sciences descriptors (DECs and MeSH), the following keywords were identified: obesity, fracture risk, osteoporosis, osteopenia. Initially, broader terms were intentionally used in order to identify a greater number of studies addressing the topic of interest and minimize the possibility of an important article being excluded from this review.

In addition, the reference lists of the primary studies included in the search were reviewed to identify possible studies that met the inclusion criteria but, for some reason, were not identified in the initial search. The following keywords were used: obesity, fracture risk, osteoporosis, osteopenia. Initially, broader terms were intentionally used in order to identify a greater number of studies addressing the topic of interest and minimize the possibility of an important article being excluded from this review.

The research question that guided the research strategy was: "Does obesity increases the risk of developing osteoporosis and the risk of fractures?"

The survey of scientific articles was carried out in the following databases and portals: MEDLINE® via PubMed®, Virtual Health Library (VHL), and Cochrane Library, using specific search strategies for each of these databases.

Prospective and retrospective studies were included, and restrictions were placed on the publication date (2017-2023) or language of the studies. They had undergone a rigorous peer review process similar to that of scientific articles. In addition, duplicate texts found by indexing in more than one database were excluded.

This stage consisted of reading and analyzing the titles, abstracts, and keywords of the identified studies. At this point, review studies and those that did not meet the objective of this study were excluded. After the initial screening, the next step was to read the studies in full. Finally, the studies were organized into tables to present their main information and facilitate a descriptive and critical analysis of the results obtained by the authors.

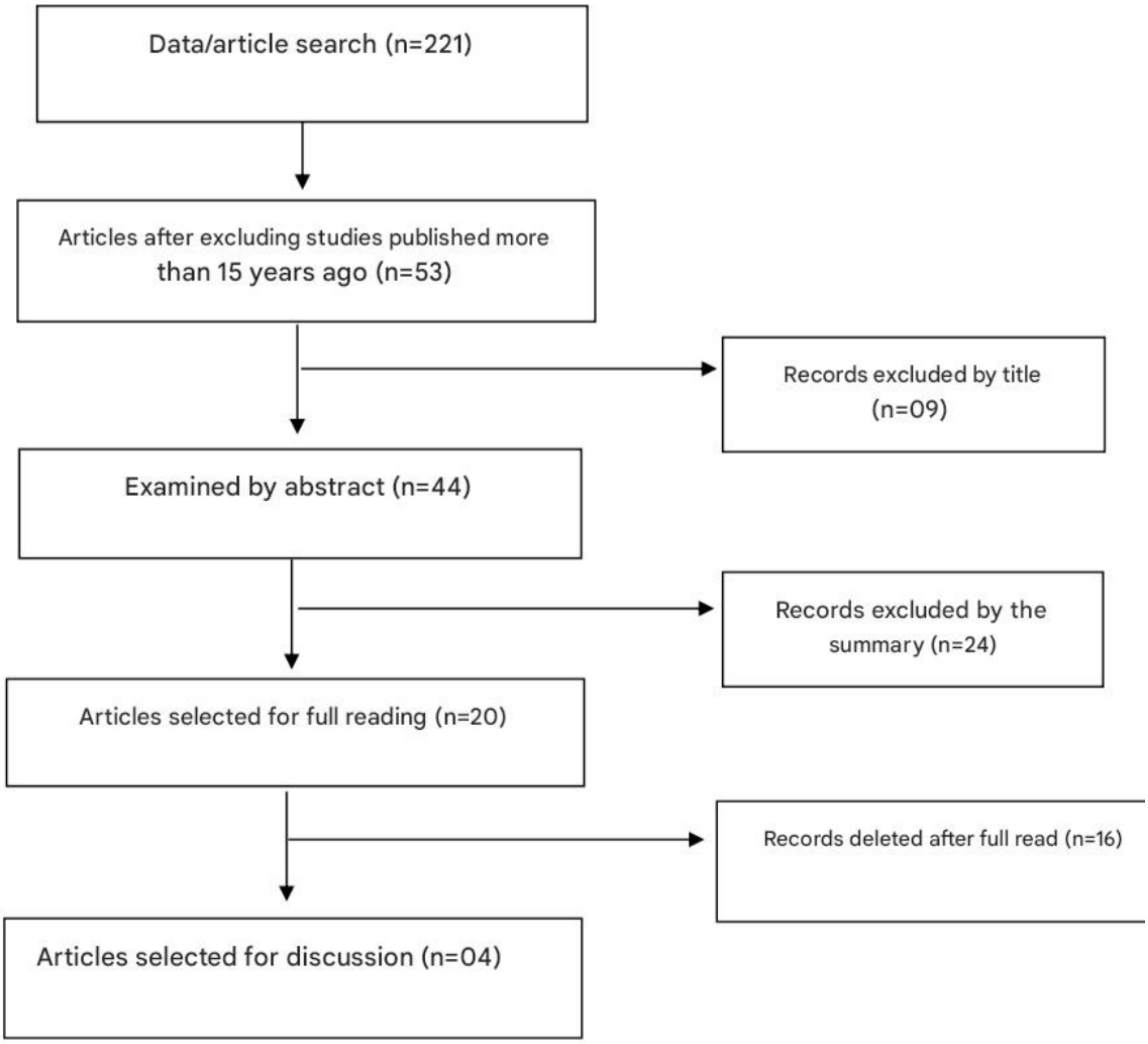
The Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) 11 was used to assess the risk of bias in the selected observational studies. The tool assesses seven domains of bias (confounding, selection, classification of interventions, deviations from proposed interventions, information, measurement of outcomes, and selective reporting of results) and classifies them as low, moderate, high, or critical risk. The overall risk of the studies was then classified as low (low risk in all areas), moderate (moderate risk in at least one area), or high (high risk in at least one area). The assessment was performed by two independent reviewers. There were no cases of disagreement that required a third assessor. Inter-rater agreement was not measured in this study. Risk of bias VISualization® (Robvis) was used to graphically present the risk of bias in the studies.

For experimental trials, the risk of bias was assessed using the Revised Cochrane risk of bias tool for randomized trials (RoB 2). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to classify the quality of scientific evidence for the results analyzed. This system was chosen because of its advantages over other evidence grading systems, namely because it allows the assessment of evidence quality to be separated from the assessment of the strength of the recommendation.

3.Results

A total of 221 articles were selected. Upon evaluating the publication date, 168 were eliminated because they had been published more than 15 years ago. Analysis of the titles resulted in the exclusion of 9 articles, and another 44 were eliminated after evaluation of the abstracts because they did not meet the objectives proposed by the study. Thus, 20 papers remained for complete reading, of which only 4 were selected because they related to the risk of fracture in overweight and obese individuals (Figure 1).

Figure 1 - Selection of studies according to the PRISMA methodology.



Source: Author's own work (2024).

The four articles selected evaluated the risk of fractures in overweight (BMI > 25 kg/m²) and obese (BMI > 30 kg/m²) patients. A total of 13,263 participants were included, with mean ages ranging from 40 to 62 years. Two studies reported the risk of ankle fractures in this population, and another two evaluated the relationship by body segment. The association with osteoporosis and lifestyle habits was also evaluated in some of the studies.

Table 1. Evaluated results of selected studies.

Study	Middle Ages	F/M patients	Body mass index (BMI) > 30	Results
Hjelle e col	40 years	240/67	33,6%	Association between overweight, obesity, osteoporosis, and ankle fracture.
King CM	52 years	180/100	69,2%	Association between overweight, obesity, osteoporosis, and ankle fracture.
Compston e col	68 years	44.534/0	23,4%	Association between obesity, lifestyle habits, and fractures by body segment.
Gnudi S	64 years	2235/0	6,8%	Association between obesity and fractures by body segment

Table 1 shows the selected studies and their outcomes. 12,13,14,15

Table 2. Analysis of fracture risks in obese patients by body location according to the studies discussed.

Fracture location	Association with obesity (%)
Ankle	10,3%
Hip	1,1%
Fish	7,6%
Arm and shoulder	3,5%

Table 2 shows the risk of fractures in obese patients by body location according to the studies reviewed. 12,13,14,15

The study by Hjelle et al. evaluated the relationship between overweight, obesity, osteoporosis, and ankle fractures. A total of 307 participants took part in the study, 108 of whom suffered ankle fractures. Of these, 27.1% had adequate body weight, 39.3% were overweight, and 33.6% were obese.Low-energy trauma was associated with 71.3% of ankle fractures in this study population. The prevalence of osteoporosis and osteopenia was similar in the ankle fracture group and in the controls (22.4% vs. 22.3% and 47.7% vs. 51.7%, respectively). Regarding lifestyle habits, 36.4% of patients with fractures were smokers and 23.1% used polypharmacy; these values for the control group were 40.6% and 21.6%, respectively. Ankle fractures were classified according to Danis-Weber (DW): 17 patients had Danis-Weber type A fractures, with 17.7% considered obese. Ninety-one had type B or C fractures; of the patients with fractures classified as B, 38% were obese, while this number for type C was 40%. 12

The study by King et al. also analyzed the relationship between obesity and ankle fractures. A total of 280 participants were included, of whom 69.2% had a BMI of 30 kg/m². According to the Danis-Weber classification, 59 had type A fractures, 165 patients had type B fractures, and 56 had Danis-Weber type C ankle fractures. Forty-five percent of patients with type A fractures were obese, this number rose to 50.3% in type B and 60.7%

for type C. Osteoporosis was associated with 20.3% of type A fractures, 9.09% of type B fractures, and 7.14% of type C fractures. Patients over 25 years of age were 1.78 times more likely to have a Weber C or Weber B or C fracture. 13

The study by Compston et al. evaluated the relationship between obesity and fractures in

postmenopausal women. The average BMI of those diagnosed with some type of fracture was greater than 30 kg/m². The data obtained for these patients, per 1,000 women, were: hip fracture in obese and non-obese women (15 versus 20.5), ankle fracture (88.6 versus 63.7), wrist fracture (79.1 versus 101.1), clavicle fracture (13 versus 14.8), upper arm fracture (35 versus 32.2), spine fracture (24.2 versus 27.9), and leg fracture (34.2 versus 26.6). Some risk factors were identified for fractures, among them early menopause and alcoholism, which were associated with a higher number of cases in obese patients, with a prevalence of 194 and 1.1 per thousand women, respectively, while non-obese women recorded numbers of 128 per thousand women with early menopause and no record of involvement between alcohol and fractures in these patients. The use of medication for the treatment of osteoporosis was lower in obese women with fractures compared to non-obese women (55.9 versus 77.6 per thousand women), respectively. 14

Gnudi et al. evaluated the relationship between obesity, osteoporosis, and fractures in postmenopausal women. Of the 2,235 women, 72% had some type of fracture.

152 were obese and 884 had a BMI < 30 kg/m². Hip fractures accounted for 3.3% of fractures in obese women and 8.2% in non-obese women, humerus fractures 7.7% in obese women versus 3.6% in non-obese women, wrist fractures 11.5% and 11% and ankle fractures 4.8% and 4.4% in obese and non-obese individuals, respectively. 15

4. Discussion

The main types of obesity-related fractures were those of the ankle and lower limbs, most often associated with low-energy trauma. Wrist and hip fractures were more commonly associated with non-obese women. Osteoporosis was associated with a significant proportion of cases, and the use of medications to treat the condition was related to a lower number of fractures in the study population. 12,13,14,15

Abdominal obesity and osteoporosis are growing at an alarming rate, increasing the possibility of bone fractures in individuals. Inflammatory cytokines (resistine, TNF-a, IL-1, and IL-6) are released by adipose tissue cells (adipocytes) and affect bone remodeling, increasing bone resorption and suppressing bone formation. In addition, adiponectin and leptin contribute to increased sympathetic impulse output in the bone, reaching the hypothalamic center that regulates sympathetic tone. These impulses reduce osteoblast differentiation, also influencing bone remodeling. 16

The relationship between obesity and the risk of bone fracture is heterogeneous and appears to vary depending on the location of the skeleton. Some studies show that bone mineral density is higher in obese patients, but they have impaired bone quality, which may be a determining factor in the risk of fracture in this group of patients. Regarding the risk of fracture by anatomical location, it was found that postmenopausal women with obesity

had a reduced risk of hip and wrist fractures by 25% and 15%, respectively, while the risk of ankle fractures increased 1.6 compared to postmenopausal women without obesity. 17

The reasons for this location-specific association are not yet fully understood, but it is known that in specific topographies, different properties of bone material can interfere with fracture resistance. Thus, the hip and wrist in obese patients may be more protected against fractures due to increased bone mineral density, which increases bone strength, whereas sites such as the vertebrae or lower limbs fracture through other means of failure.

14,15

Although obese individuals are more prone to falling due to reduced mobility, postural control, and protective responses, the accumulation of fat around the hip area can aid in energy dissipation after trauma, contributing to a decrease in hip fractures. In addition, the pattern of falling in individuals with and without obesity is different, as obese patients are more likely to fall backward or sideways rather than forward. Thus, the wrists are less exposed to trauma, which may explain the higher risk of fracture in this location. 18

Another possible reason is that the ankles are not protected by fat and have to bear more body weight when falling, explaining the increase in fractures in this area. 15 Thus, in order to reduce the impact of obesity on bone remodeling,surgical intervention was considered as a way to reduce the patient's BMI more quickly. 15

However, according to studies that evaluated dual-energy X-ray absorptiometry(DXA) and quantitative computed tomography (QCT) after bariatric surgery, there is a decline in bone mineral density, leading to negative effects on bone health. Other fracture-related characteristics were observed in relation to bariatric surgery, such as the risk of fracture after the surgical procedure being site-dependent, mainly affecting the distal lower limb, and an increased risk of osteoporotic fracture, suggesting that the deleterious changes to the bone during surgery are systemic in nature. 15

5. Conclusion

The relationship between obesity and bone fracture risk is heterogeneous and appears to vary depending on the location of the skeleton. Ankle fractures were the most commonly associated with obesity, while in areas such as the hip, the accumulation of fat around the bone may aid in dissipating energy after trauma, contributing to a decrease in fractures in these regions.

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