Fracture risk in obesity: a narrative review

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Abstract
While low body mass index (BMI) is a risk factor for fractures, the association between obesity and fracture risk is inconsistent and puzzling. Several studies reported higher fracture risk (FR), and others reported lower FR in obese populations. Our narrative review presents the overall incidence of fractures by anatomic locations in adult patients, geriatric populations, and in those after bariatric surgery. In conclusion, obesity should be considered as a fracture risk in adults, as well as falls and fractures in geriatric patients, in particular in those with sarcopenic obesity, and after bariatric surgery. The specific characteristics of fractures risk associated with obesity should be considered by physicians in the diagnostic and therapeutic work-up of obese patients. This review outlines the current literature on this topic and aims to guide physicians regarding proper decisions to prevent fractures in patients with obesity. (Endokrynol Pol 2022; 73 (5): 885–892)

Key words: osteoporotic fracture; alimentary obesity; sarcopenic obesity; bariatric surgery

Introduction
Obesity is a significant worldwide health problem because of its associations with diseases such as diabetes mellitus, arterial hypertension, heart failure, coronary artery disease, and cancer. Additionally, obesity is associated with hypovitaminosis D and the risk of osteoporosis and fractures. This is important because low body weight [body mass index (BMI) < 18.5 kg/m²] is usually one of the fundamental risk factors for the development of osteoporosis/low bone mass and is associated with increased fracture risk (FR) [1].

Obesity is a condition of increased body weight (BMI > 30 kg/m²) due to excessive accumulation of adipose tissue in the body because of adipocyte hypertrophy and/or hyperplasia. Over 90% of cases of this disease result from hyperalimentation, and the remaining 10% from secondary causes of obesity [2]. For practical reasons, the most useful indicators for the diagnosis of obesity are simple anthropometric measurements, such as the BMI or the waist/hip ratio (WHR). Unfortunately, anthropometric measurements do not assess the amount/mass of adipose tissue and only indirectly indicate its excess or deficiency. Electrical bioimpedance seems to be slightly better, and imaging tests, e.g. densitometry (DXA) or computed tomography (CT), which provide information on the composition of the whole body, are much more accurate.

Opinions on the beneficial effects of obesity on the skeletal system are divergent because there are a number of arguments for and against this hypothesis. It is important to stress that opinions were the result of different methods to assess obesity and different populations. Therefore, the aim of this narrative review is to focus on the estimation of fracture risk in patients with obesity caused by hyperalimentation, adults, seniors, and after bariatric surgery and the indication of specific treatment features in these populations.

Fracture risk in alimentary obesity
The FR appears to be influenced not only by the weight itself from excess body weight (anthropometric parameters), but also by the relative or absolute weight or amount/volume of adipose tissue associated with it or with its distribution (body composition). In this context, more information on the FR in obesity may be provided by bone mineral density (BMD), CT, the mass of adipose and lean tissue, as well as their mutual proportions. This seems to be significant, especially in premenopausal...
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and postmenopausal women. Next, we discuss the relationship between anthropometric parameters, body composition, and FR in obesity.

**BMI and fracture risk**

In one study, a large population of women ≥ 50 years of age, who had BMI measurements at least once, were analysed retrospectively. Hip and pelvis fractures were significantly less frequent in overweight and obese women compared to healthy or weight-deficient women. By contrast, obese women had a significantly higher risk of humerus fractures compared to the underweight/normal-weight group [3]. In a meta-analysis of 25 prospective observational studies, Johansson et al. included a large female population of women aged 20 to 105 years [4]. The incidence of obesity (BMI ≥ 30 kg/m²) was 22%. The authors showed that both low and high BMI can be a risk factor for fractures. Low BMI was a risk factor for all osteoporotic fractures (including hip fracture) but proved to be a protective factor for vertebral fractures. These findings suggest that fat distribution may have a significant impact on the risk of vertebral fractures and that central/abdominal obesity should be avoided and muscle mass should be maintained. Other research has shown a similar relationship for hip fractures [7]. Indeed, the risk of hip fracture increases by about 3.0% [95% confidence interval (CI): 1.0–4.0%] for each 0.1-unit increment of WHR [8].

**BMD, CT, and fracture**

It seems that fat mass is a better determinant of BMD of the lumbar spine, and LBM has a greater effect on hip BMD [9]. The described relationships between BMD and fat mass and LBM in the case of FR are not consistently reported, especially in cross-sectional studies [10, 11]. Dolan et al. included in their meta-analysis 16 clinical trials [12]. Participants were divided into 3 age groups: < 25 years (n = 713), 25–55 years (n = 618), and > 55 years (n = 1256). Higher adipose tissue mass, and therefore body weight, was associated with higher BMD values. The higher relative mass of adipose tissue in overweight or obese populations was negatively correlated with bone mass, particularly in men and in the group < 25 years of age, which probably occurred when accompanied by lower LBM. Sheu et al. studied the relationship between the amount of subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), intermuscular abdominal fat (IMAF), muscle volume, and the incidence of vertebral fractures in a male elderly population [13]. These tissue parameters were measured using quantitative CT at the level of the L4/L5 intervertebral space. Three groups of muscles and the fat between them were assessed: the total abdominal, psoas, and paraspinal muscles. The authors determined that a 1 standard deviation (1-SD) increase in psoas muscle volume, but not paraspinal muscle, was associated with a 28% lower FR. Regarding the presence of fat mass, only a higher intramuscular adipose tissue (IMAT) of the total abdominal muscle contributed to a greater FR in older men regardless of BMD. Another study of the elderly population found that the femoral muscle density attenuation in the CT imaging measured by DXA [an increase in the LBM index in the appendicular area divided by the square of height, lean mass index (LMI)], as well as a decrease in the subcutaneous fat thickness, were associated with greater risk of hip fracture in men [14]. For women, only a reduction in the subcutaneous fat thickness and the cross-sectional area of the thigh muscles were associated with an increased risk of hip fracture. Surprisingly, men with high LMI and low subcutaneous fat thickness had a more than 8 times higher risk of hip fracture compared to individuals with low LMI and high subcutaneous fat thickness. Zheng et al. used a similar methodology to analyse data from a Swedish cohort study of patients with normal
body weight, overweight, and obesity [15]. The authors estimated the fracture hazard ratio (HR) for baseline BMI and its change of at least 0.5 kg/m² over the previous 12 or 18 years, baseline WHR, and, as assessed by DXA, total and regional fat distribution and LBM, with or without adjustment to local BMD. Summarizing the results, FR in both sexes was most influenced by low baseline BMI, prior BMI loss, and abdominal obesity. Another prospective cohort study focused on the evaluation of LBM and fat mass percentage (%F) using the electrical bioimpedance method [16]. Cases of low-energy fractures were assessed at baseline and every 2 years. The researchers found that men with low LBM with normal and high %F had > 2 times higher FR, respectively, than men with normal parameters, even after adjusting for covariates. Interestingly, in women low LBM or high %F was not associated with FR. Other researchers found that an increase in the amount of adipose tissue assessed by DXA was accompanied by a higher incidence of pelvic and femoral fractures [17]. These results were still significant after considering the patients’ BMI.

An interesting approach for assessing the relationship between body composition and bone strength was presented by Leslie et al. [18]. The researchers analysed the body composition of elderly patients during DXA of the hip and spine, and based on the developed mathematical formulas, they calculated, among others, the total body fat and LBM and bone strength indicators (SI). Unfortunately, there was no evidence that LBM, fat mass, or SI of the femur could predict major and hip fractures (FRAX values with or without BMD). The results were similar for men and women, with no relation to obesity. Higher fat mass was not independently associated with a higher FR over 5 years of follow-up. However, researchers from the same site used the same methodology and found that the loss of total LBM was statistically greater in people with new fractures in the hip and major locations, while the loss of fat mass was significantly greater only in patients with new fractures of the femoral neck [19]. In addition, a 1-SD loss of LBM was associated with a 10–13% higher risk of major fractures and a 29–38% increased risk of hip fracture corrected for fat loss and other covariates. Prior fat loss was not associated with new fractures after adjusting for LBM loss. In the elderly population, it is probable that lean body mass is just one of the factors that should be considered, and muscle strength and function could become distinctive characteristics for FR risk estimation.

In patients with alimentary obesity the treatment of overweight is still not well established, and there is no consensus concerning obesity treatment from the perspective of fracture risk.

**Prophylaxis and treatment**

In our opinion, the risk of future fractures in adult patients with osteoporosis and alimentary obesity should be determined using country-specific assessment tools to guide decision-making. Patient preferences should be incorporated into treatment planning.

Nutritional and lifestyle interventions and fall prevention should accompany all pharmacological regimens to reduce fracture risk. Multiple pharmacological therapies can reduce fracture rates in these groups with acceptable risk-benefit and safety profiles [20]. Vitamin D plays an important role, and in obese people (BMI > 30 kg/m²) the daily dose is 3 times higher than the recommended dose in people with normal body weight. Treatment doses are indicated when the vitamin D concentration is below 20 ng/mL (see below) [21, 22].

Preventive treatment: European recommendations for osteoporosis note that a history of fracture not caused by a major trauma, and a low BMD are the most important risk factors for fractures. However, additional clinical risk factors contribute to fracture risk [23]. Very high fracture risk and the consequent utility loss immediately after a fracture (often termed “imminent risk”) suggests that preventive treatment given as soon as possible after a fracture would avoid a new fracture and reduce the attendant morbidity, compared with a treatment given later. This is the rationale for early intervention immediately after a sentinel fracture, and it necessitates treatment with agents that have the most rapid effect on fracture reduction (anabolic therapy if it is impossible to start with antiresorptive treatment). According to the European recommendations, postmenopausal women and elderly men with a prior fragility fracture should be treated without further assessment, although BMD measurement and incorporation into the FRAX calculation is sometimes appropriate, particularly in younger postmenopausal women.

In women and men without a previous fragility fracture, the management strategy should be based on the assessment of the 10-year probability (RB-10) of a major osteoporotic fracture (clinical spine, high forearm, or humerus). In the Polish population, RB-10 upper 10% can be considered for treatment; RB-10 between the upper and lower (5–10%) assessment threshold should be referred for BMD measurements and the reassessment of fracture probability. Patients with RB-10 below 5% can be considered at low risk [24].

The drugs approved in Poland for the treatment of osteoporosis are only agents acting through inhibition of osteoclastic bone resorption. The orally administered bisphosphonates alendronate and risedronate, the intravenously administered bisphosphonate zoledronic acid, and denosumab, the subcutaneously administered monoclonal antibody neutralizing the ac-
tivity of human receptor activator of nuclear factor-kB (RANKL), are all “anti-resorptive” bone-active. Anabolic bone active agents with bone-forming properties, such as teriparatide, abaloparatide, and romozosumab, are not available in Poland. It has been shown that the effectiveness of antiresorptive and anabolic treatment is more effective when the levels of calcium and vitamin D are within the normal range [25]. For patients with vitamin D deficiency (25[OH]D lower than 20 ng/mL [50 nmol/L]), a vitamin D treatment should be introduced; for adults and the elderly 7000–10,000 IU/d or 50,000 IU/week for 6–12 weeks [26, 27].

Fracture risk in sarcopenic obesity patients

Obesity in patients aged ≥75 years or above is a special problem in view of the high risk of sarcopenic obesity (SO).

The definition of SO is based on the coexistence of 2 processes: loss of muscle mass and function, and increased fat mass. Many studies confirm that the relationship between obesity and sarcopenia in terms of morbidity and functional decline (which exacerbate the risk of falls and fracture) provides a worse prognosis than these conditions alone in obese older adults.

Currently, there are well-established cut-off points that define sarcopenia; however, there is no consensus regarding SO. Baumgartner et al. were among the first researchers to highlight the association of SO with functional decline. Obesity in sarcopenic individuals was defined as appendicular skeletal percentage of body fat greater than the 60th percentile of the study sample. The authors found that all subjects with SO at baseline were 2 to 3 times more likely to report incident disability (relative risk being 2.63) during follow-up when comparing sarcopenic or nonsarcopenic obese older people to those with normal body composition [28]. The last decade produced a wide range of studies in this field, and currently the use of DXA seems to be the “gold standard” because BMI alone or WHR may not reflect the amount of body fat in the elderly [29].

The heterogeneity of the current diagnostic criteria for obesity in older adults leads to a significant variation in the estimated prevalence of SO and simultaneously its impact on other adverse health outcomes such as falls and fractures. The prevalence increases with age but is extremely variable, and this diversity depends on the applied definition [30]. A multifactorial diagram of SO causes and effects is shown in Figure 1.

Falls and fractures

Falls may result in post-fall syndrome or/and injuries, of which over 60% constitute bone fractures with the most common and devastating being hip fractures [31]. Some studies have shown that sarcopenic, obese subjects have not only an increased risk of falls and FR, but also poor balance [32]. The phenomena of balance destabilization may be one of the mechanisms promoting an increase in fall risk [33]. Simultaneously, progressive functional decline contributes to a higher risk of falls.

Figure 1. Sarcopenic obesity — causes and effects
and FR, and it has been proven that sarcopenic obesity correlates with an increased risk of severe decline of physical performance. Follis et al. conducted a prospective study focused on the relationship between SO and falls in 11,020 postmenopausal women aged from 50 to 79 years. They showed that SO was associated with a higher risk of falls in the whole group [34].

A cross-sectional study provided by Lee et al. showed that SO could be used as a negative prognostic factor—a fracture fragility indicator for acute vertebral osteoporotic compression fractures [35]. The authors documented that individuals with sarcopenic obesity (especially women) have a significantly higher risk of acute vertebral osteoporotic compression fractures in comparison to sarcopenia or obesity alone, as well as in comparison to individuals with normal body mass. A recent systematic review (26 studies, n = 37,124) and meta-analysis (17 studies, n = 31,540) on this topic was published by Gandham et al. [36]. It was reported that older adults with SO had significantly higher areal BMD (aBMD) in comparison to sarcopenic individuals, but significantly lower aBMD compared with individuals with obesity alone. They demonstrated a 30% higher risk of falls compared with controls, and a 17% greater risk of falls compared to obese individuals. Importantly, individuals with sarcopenic obesity had an 88% greater nonvertebral fracture rate compared to subjects with sarcopenia alone. The authors highlighted that the geriatric population with sarcopenia coexisting with obesity are at greater risk of adverse musculoskeletal and functional outcomes. The pathogenesis of this phenomenon is complex and multifactorial but might be partly explained by higher body weight, which provides greater mechanical loading of bone, but also poorer bone quality should be considered, especially when coexisting with muscle strength and function loss [37].

**Prophylaxis and treatment**

**General recommendations referring to SO**
The higher risk of falls and FR in patients with SO compared to patients without SO indicates that the first step should be screening for the high risk of falls and gait disturbance, for example with a timed up and go test (TUGT), and at the same time screening for SO to determine the high-risk subpopulation of osteoporotic fractures (FRAX, DXA). This clinical profile may lead clinicians to intervene with a combination treatment intervention. Sarcopenic obesity treatment is based on physical activity, adjusted diet, and vitamin D supplementation in vitamin D-deficient individuals.

Physical training should consist of regular resistance training and aerobic exercises accompanied by everyday balance training. The efficacy of such training is higher in older individuals not only because of muscle strength and function amelioration but also because of fall reduction. Simultaneously, the diet should be focused on high protein intake with slight body mass reduction [38]. Therapeutic strategies with effective pharmacological agents on SO with a history of osteoporotic fracture, low BMD, and high 10-year probability of osteoporotic fracture (RB-10) can be considered (see Prophylaxis and treatment).

**Fracture risk after bariatric surgery**
The relevance of bariatric surgery is growing with the current obesity pandemic. Bariatric procedures are not only the most effective methods to reduce excess weight but also allow for the improvement or even remission of most obesity-related comorbidities. However, the surgery itself constitutes a serious interference with the organism’s homeostasis and is associated with the risk of both acute and chronic complications.

**Consequences of bariatric surgery**
The negative health consequences of bariatric surgery are more pronounced with malabsorptive procedures (e.g. Roux-en-Y gastric bypass — RYGB, biliopancreatic diversion — BPD, biliopancreatic diversion with duodenal switch — BPD-SD), and less significant in restrictive ones (e.g. sleeve gastrectomy — SG, adjustable gastric banding — AGB) [39].

**Fracture risk**
Concerning bone tissue, bariatric surgery harms BMD and microarchitecture. The mechanisms underlying this deleterious effect upon bone quality are varied and not yet fully understood (Fig. 2).

**Fracture risk and bariatric surgery**
At the beginning of 2022, two meta-analyses were published comparing the risk of fractures in adult patients undergoing bariatric surgery to those in sex- and age-matched, non-surgically treated obese individuals. The first meta-analyses, by Chaves Pereira de Holanda et al., included 15 studies: 12 observational and 3 interventional, and noted a significantly higher prevalence of fractures in the intervention group (3512 events in 138,562 bariatric patients) compared to the group of the control subjects (3512 events in 156,994 non-surgically treated individuals). The relative risk (RR) of any type of fracture associated with bariatric procedures was 1.20 (95% CI: 1.15–1.26). Moreover, the risk of any type of fracture was significantly higher in the case of malabsorption procedures (RR: 2.11, 95% CI: 0.72–2.58), while restrictive surgery did not entail an increased risk of fractures compared to the non-
surgical procedures (RR: 1.04, 95% CI: 0.89–1.23) [40]. The second meta-analysis, by Saad et al., covered 15 observational and 4 interventional studies and yielded similar results. In observational studies, the RR of any fracture was 45% higher following malabsorptive surgery than in non-surgically treated controls and 61% higher than after restrictive procedures. The most common fracture sites in patients after bariatric surgery were the hip and wrist, while the incidence of vertebral and humerus fractures did not differ significantly between the study groups. The site-specific relative fracture risk (hip and wrist) was one to two times higher after malabsorptive procedures compared to non-surgically treated obese individuals or restrictive surgery. The risks of site-specific fracture were not increased following restrictive procedures compared to non-surgically treated controls. The period when any type of fracture risk becomes significant was estimated to be 2 years after the procedure [41]. However, the moment of increased fracture risk after bariatric procedures may vary, depending on location. The risk increases for wrist and hip fractures during the second year after the procedure, while in the case of the distal lower limb and vertebral fractures, after approximately 3 and 10 years, respectively.

In summary, bariatric surgery has an impact on bone fracture sites, changing the pattern from the one associated with obesity (distal lower limb) to a pattern typical of osteoporosis after surgery (upper limb, spine, pelvic, hip, and femur fractures) [42].

**Prophylaxis and treatment**

Supplementation with vitamin D, calcium, and BMI-adjusted protein decelerates the loss of BMD and LBM after bariatric surgery, and it should be tailored according to the patient’s laboratory tests.

The general recommendations refer to bariatric patients with normal body mass

The average postoperative consumption of elemental calcium is 1200–2000 mg/day, and supplementation with 3000 IU/d of vitamin D for patients without preoperative deficiency of this vitamin. However, individuals with severe vitamin D malabsorption may require up to 50,000 IU of vitamin D administered 3 times a week [43]. The adequacy of postoperative calcium
and vitamin D supplementation should be regularly verified. As well as nutritional interventions, regular physical activity, including weight-bearing and aerobic exercises, should be recommended to all individuals after bariatric surgery to improve BMD and prevent a decrease of LBM [44].

Therapeutic strategies for bariatric surgery-induced bone loss management are limited. They are based on expert opinions rather than the results of randomized controlled trials. Osteoporosis treatment should be considered in postmenopausal women and men > 50 years old if any of the following criteria are present: — recent history of fragility fracture > 40 years of age; — T-score ≤ −2 at the hip or spine; — FRAX score with femoral neck BMD exceeding 20% for the 10-year major osteoporotic fracture probability or exceeding 3% for hip fracture.

For many years, oral bisphosphonates have not been recommended due to the risk of anastomotic erosions and potential hypocalcaemia, and intravenous zoledronate has been the only option. A prerequisite for the safe use of zoledronate is adequate calcium and vitamin D supplementation [45]. In patients after SG the safety and efficiency of oral risedronate in the management of osteoporosis are currently being tested in a clinical trial. Other possible therapies for bariatric surgery-induced osteoporosis include the use of raloxifene (a selective oestrogen receptor modulator — SERM) in postmenopausal women, a parathyroid hormone (PTH) analogue — teriparatide (regardless of the hypoparathyroidism), and denosumab. Additional benefits of treatment with denosumab include its favourable effect on gut hormones [glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP)], which translates into improvement of glucose homeostasis. Nevertheless, none of these therapeutic strategies has been sufficiently verified in clinical trials [46].

Conclusion

The aim of this work was to provide a systematic literature review on the topic of fracture risk in adult patients with alimentary obesity, and to draw attention to gaps and inequalities in the provision of primary and secondary prevention of fractures due to osteoporosis.

It is important to stress that the fracture risk for patients with obesity caused by hyperalimentation, aging, and after bariatric surgery is greater than in patients with normal weight. Despite the complex and multifactorial pathogenesis of these results, physicians must decide on a specific treatment for patients in these populations.

In alimentary obesity, the treatment for weight loss is yet to be well established, and there is no consensus concerning obesity treatment from the perspective of fracture risk.

In our opinion, the risk of future fractures in adult patients with osteoporosis and alimentary obesity should be determined using country-specific assessment tools to guide decision-making.

According to the Polish recommendations for diagnostic and therapeutic strategies on patients with a history of osteoporotic fracture, low BMD, and high 10-year probability of osteoporotic fracture (RB-10), pharmacological treatment can be considered. Multiple pharmacological therapies can reduce fracture rates in these groups with acceptable risk-benefit and safety profiles.

Nutritional and lifestyle interventions, and fall prevention should accompany all pharmacological regimens to reduce fracture risk. Also, improvement of vitamin D and calcium concentrations to reference levels plays an important role.

These non-pharmacological interventions should be individually considered based on the patient’s general condition and other treatments for obesity.

The drugs approved in Poland for the treatment of osteoporosis are the only agents that act through the inhibition of osteoclastic bone resorption. These are the orally administered bisphosphonates alendronate and risedronate, the intravenously administered bisphosphonate zoledronic acid, and denosumab. Anabolic bone active agents with bone-forming properties, such as teriparatide, abaloparatide, and romozosumab, are not available in Poland.

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None declared.

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