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ORIGINAL ARTICLES

Obesity and osteoporotic fractures

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Abstract: *Obesity correlates with a higher risk of fractures in some sites as vertebras, upper arm, and legs. This is a narrative mini-review focused on several key points that link obesity with osteoporosis. Waist circumference may a better predictor of fractures than body mass index (BMI) in obese females. Even obese menopausal women have an extra source of estrogens in fat tissue this actually is not enough to offer a complete protection against osteoporotic fractures. Low levels of testosterone in males induce a higher risk of fall dependent or independent of sarcopenia (which is more evident in elderly). High BMI is correlated with vitamin D deficiency. Obesity is a contributor to muscle damage and decline due to fat accumulation and inefficient fuel utilisation by the muscle, namely sarcopenic obesity, regardless the age. Associated type 2 diabetes mellitus involves bone damage and fracture risk due to glycated proteins of the matrix, the changes of adipokines, increased cortical porosity, high risk of fall because of blood pressure and glycaemia anomalies, visual disturbances, renal and peripheral nerves diabetes-associated conditions etc. The fracture risk is also augmented via fat derived cytokines and chronic inflammation. Even it seems logical that the weight correction though bariatric surgery reduces the fracture risk in obesity, actually data from longitudinal studies pointed that, despite the procedure is life saving, it does not actually protect against osteoporosis which is regarded as a potential long-term complication. A high fracture burden in obesity should increase the level of awareness for practitioners of different medical areas due to multiple levels of complications and to the epidemiological impact of obesity.*

Keywords: *obesity, osteoporosis, fracture*

INTRODUCTION

Obesity currently represents a pandemic issue and every medical and surgical speciality includes different complications of obesity from cardiovascular conditions, type 2 diabetes mellitus and insulin-resistance, some types of cancer to infections at any level including skin, lungs, urinary tract, gastrointestinal infections, respective infertility, sleep apnoea, non-alcoholic fatty liver disease, depression, and finally any of these or their combination may increase the overall mortality. [1, 2, 3, 4] The increasing epidemiological impact has brought a large area of concern worldwide. [1, 2, 3, 4] The endocrine frame of obesity perception is related to hypothyroidism, hypercortisolemia, male hypogonadism, female hyperandrogenemia, and lately to osteoporosis and fragility fractures, including hypovitaminois D. [5] A systematic review associated with a meta-analysis published in 2019 by van Hulsteijn et al. included 68 studies (meaning 19,996 obese subjects). [6] The study identified that 28% of the individuals had reduced thyroid function of different severities, while 0.9% of them had hypercortisolemia. [6] When it comes to males the prevalence of hypogonadism was between 32 and 42%

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depending on criteria. [6] Contrary to historical records that consider obese women protected against osteoporosis because of the estrogens excess at the level of adipose tissue, last two decades brought enough proves that actually this hypothesis is not entirely true. [7]

AIM

Our purpose is to introduce data related to the risk and prevalence of osteoporotic fractures in obese persons.

MATERIAL AND METHOD

This is a narrative mini-review of the literature based on a research focused on several practical key points that correlate obesity with osteoporosis. A number of 69 articles have been included in the selection.

RESULTS – GENERAL DATA

The influence of abdominal obesity versus body mass index

The link between obesity and fractures may be expressed as BMI (Body Mass Index), either as abdominal obesity. A cross-sectional study published in 2019 showed that among 669 elderly women 65 had fragility fractures of different sites, with an average age of 73.9 years. [8] BMI was not associated with fragility fractures but abdominal obesity suggested by a waist of more than 88 centimetres (cm) was, regardless the presence of different clinical risk factors as smoking or age etc. [8] Some authors suggested that actually the waist circumference is a better predictor of fractures than BMI in overweighed and obese females. [8,9] It seems that low body mass index as well as high content of body fat, respective increase BMI both are associated with high fracture risk, especially at vertebral site. [9] Generally the fat content of the body has been reported as an accurate predictor factor for several conditions including cardiovascular and metabolic morbidities. [10] On the other hand, the influence of BMI on osteoporotic fractures risk may include the fact that low and high BMIs are considered at risk for fractures despite Bone Mineral Density (BMD) values which are directly correlated with BMI and it might not reflect the real fracture risk in obese individuals. [11, 12]

Postmenopausal women

The female individuals in menopause suffer of estrogens deficiency related to menopause thus causing bone loss and low trauma fractures. [13, 14, 15] Even obese menopausal women have a second source of estrogens in fat tissue which is superior to normal weighted subjects this actually is not enough to offer a complete protection against osteoporotic fractures. [13, 14, 15] Some studies pointed a similar rate of fractures in menopausal women regardless they were obese or not and others showed a different distribution depending on site, for instance: a high risk is for vertebral fractures, humerus, upper arm, leg and ankle while a low risk has been described for hip and wrist. [13,14,15] This aspects are most probably related to the physics of fall depending on weight. [13, 14, 15]

Male hypogonadism

Even osteoporosis is less frequent in males, the prevalent fractures are found in obese men through associated hypogonadism independent of the BMI values. [16, 17, 18] Low levels of testosterone induce a higher risk of fall dependent or independent of sarcopenia (which is more evident in elderly). [16, 17, 18] Testosterone therapy may reduce the fracture risk. [16, 17, 18]

Hypercortisolemia

Glucocorticoid osteoporosis is a well known cause of obesity-related type of secondary osteoporosis. [19, 20, 21] The obese subjects without Cushing's syndrome display chronic high values of basal cortisol which seems suppressible at dexamethasone inhibition test. [19,20,21] Chronic autonomous secretion of cortisol is identified in patients with adrenal incidentaloma with an age-dependent incidence and this has been reported to increase the risk of osteoporosis independent of age. [22, 23, 24]

Hypovitaminosis D

The interest in the area of hypovitaminosis D has been explosive during the last decades. A higher BMI is positively correlated with a high risk of vitamin D deficiency based on large epidemiological studies. [25, 26, 27[However, there is still a matter of debate regarding which is the cause and which is the effect. [28, 29, 30] The potential causes of vitamin D lack include: the relative immobility and decreased sun exposure, lower dietary intake, decreased intestinal absorption, high accumulation of vitamin D at the level of adipose tissue since it is a liposoluble vitamin thus a lower bioavailability of the vitamin D. [31, 32, 33] Decreased levels of 25-hydroxivitamin D are contributors to impair muscle resistance and to sarcopenia, thus increasing the risk of fall, and finally the risk of fracture. [34, 35, 36] Also, hypovitaminosis D is a contributor to metabolic disturbances as insulin resistance, hyperlipemia etc. [37, 38] The doses of vitamin D required for supplementation are usually two to three times higher in obese versus non-obese individuals due to fat accumulation. [39, 40]

Sarcopenic obesity

The loss of muscle mass and function is progressive since the

age of 40 and accelerated after 60 years. [41, 42] Obesity is a contributor to muscle damage and decline due to fat accumulation and inefficient fuel utilisation by the muscle, namely sarcopenic obesity, regardless the age. [41, 42] The collateral contributors to this pathological status is represented by low 25-hydroxivitamin D levels and the presence of glucose metabolism anomalies. [43, 44] Overall, the weakness of muscles causes a higher risk of fall thus of fractures. [43, 44]

Type 2 diabetes mellitus

The metabolic anomalies are associated as seen in metabolic syndrome where obese individuals are also diabetics. [45, 46] The risk of fracture caused by type 2 diabetes mellitus is more evident in menopausal women. [45, 46] Type 2 diabetes is associates bone damage and high fragility fracture risk due to glycated proteins of the matrix, the changes of adipokines as leptin, increased cortical porosity, increased risk of fall due to blood pressure anomalies, visual disturbances, renal and peripheral nerves diabetes-associated conditions. [47, 48, 49, 50]

Chronic inflammation

The network between fat and bones includes anatomical aspects like high BMI associates high BMI or mechanical loading is protective for fracture, but also changes of the skeleton micro-architecture in obese subjects that differs with the skeleton site thus some types of osteoporotic fractures are more exposed. [51, 52] Moreover, the fracture risk is augmented via fat derived cytokines and chronic inflammation as seen in metabolic syndrome or abdominal adiposity. [51, 52]

Bariatric surgery

Even it seems logical that the weight correction though bariatric surgery might reduce the fracture risk in obese individuals, actually data from longitudinal studies pointed that, despite the procedure is life saving, it does not actually protect against osteoporosis. [53, 54] Why? Because of the changes involving the mechanical loading due to the weight decrease, of lower intestinal surface for nutrients absorption (including potential malabsorption), anomalies of gut-produced calcitropic hormones, and restrictive diets after surgical procedure etc. [55, 56] Even osteoporosis after bariatric surgery seems a small price to pay, the post-operatory fractures are currently regarded as a long term complication on patients of different ages. [57, 58]

Depression

A higher risk of depression has been reported in obesity. [59] This may further involve reduced physical activity, including decreased sun exposure with risk of hypovitaminosis D and other factors leading to higher risk of fall and fractures. [60] Some mediators anomalies (as well as antidepressants-related) including serotonin have been reported at risk of bone loss through peripheral changes of its concentration despite the fact that circulating 5-hydroxytriptamin has not been yet indicated as a useful bone turnover marker in daily practice and conditions with pathological increase of the molecule as neuroendocrine tumours are not conventionally on the list of secondary osteoporosis. [61, 62]

DISCUSSIONS

Fracture risk assessment

DXA (Dual-Energy X-Ray Absorptiometry) does not particularly reflect the fracture risk in obese individuals since high BMI is correlated with high BMD. [63] FRAX also uses as input BMI. [64] Bone turnover markers might be blunted in associated diabetes and dramatically increased after bariatric surgery. [65, 66] Also type 2 diabetic menopausal women may beneficiate from TBS (Trabecular Bone Score) analysis. [67] The assays of 25-hydroxivitamin D might also be useful. [68]

Current limits

Obese individuals are less likely to receive anti-osteoporotic drugs since they already have several non-osteoporotic complications requiring different therapies. [69, 70, 71] Also, if a specific advisable drug in these subjects should be used in order to treat osteoporosis and/or to prevent fractures is not clearly understood up to this moment which is that drug, and probably the therapy for osteoporosis should be done based on similar protocols as in normal weight subjects with osteoporosis. [69, 71] Moreover, higher doses of vitamin D are necessary in obesity. [69, 71] The importance of therapy in order to provide an adequate primary and secondary intervention regarding osteoporosis is essential since the complications of fractures may become more severe due to obesity co-morbidities. [69, 71, 72]

CONCLUSION

A high fracture burden in obesity should increase the level of awareness for practitioners of different medical areas due to multiple levels of complications and to the epidemiological impact of obesity.

Abbreviations:
BMI = Body Mass Index
BMD = Bone Mineral Density
cm = centimetres
DXA = Dual-Energy X-Ray Absorptiometrry
TBS = Trabecular Bone Scor

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