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SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté,
de mes chers condisciples
et selon la tradition d'Hippocrate,
je promets et je jure d'être fidèle aux lois de l'honneur
et de la probité dans l'exercice de la Médecine.

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et n'exigerai jamais un salaire au-dessus de mon travail.

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à corrompre les mœurs ni à favoriser le crime.

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ABREVIATIONS

BMC: bone mineral content

BMI: body mass index

BMD: bone mineral density

DMO : Densité Minérale Osseuse

DXA : dual-energy X-ray absorptiometry / Absorptiomètrie biphotonique à rayons X

FM: fat mass

TUG : timed up and go test

6MWT: 6-minute walking test

pQCT: peripheral quantitative computed tomography

WC: waist circumference

RESUME

Introduction: L'ostéoporose, est une condition liée à l'âge conduisant aux fractures de fragilité avec des conséquences en termes de morbidité, mortalité et sociétale. Même si avoir un faible indice de masse corporelle (IMC) est un facteur de risque reconnu de fragilité osseuse, l'impact de l'obésité sur l'os (densité et architecture) est. elle contradictoire. Une des raisons possibles serait que l'IMC qui définit l'obésité est avec l'âge un marqueur imparfait. Ainsi, d'autres marqueurs cliniques du tissu adipeux (pourcentage de masse grasse (MG) ou tour de taille (TT)) devraient être explorés.

Objectif: 1) Examiner la corrélation entre les différentes mesures d'obésités et les paramètres osseux; 2) Comparer les paramètres osseux entre des aînés obèses et non-obèses selon 3 critères d'obésité

Méthodologie: Étude transversale incluant 145 hommes (H; n=91) et femmes (F; n=54) âgés de 55 à 80 ans, sédentaires et habitants au Québec (Canada). Les participants ont été classés obèses ou non selon 3 paramètres: l'IMC (>30kg/m^2), le TT (F>80cm; H>94cm) et le pourcentage de MG (F>40%; H>27%). La composition corporelle (grasse, osseuse et musculaire) ont été recueillis via un ostéodensitométrie (DXA) et un CT-scan périphérique (QPCT; XCT-3000).

Résultats: Parmi les 145 sujets inclus, 44 (30%) étaient obèses selon l'IMC, 95 (65%) selon le pourcentage de MG et 119 (82%) selon le TT. Les patients obèses selon le TT et le % MG avaient des paramètres osseux moins favorables que ceux non-obèses. En revanche, cette observation était inversée pour ceux classés obèses selon l'IMC. Au niveau des corrélations, seul le % de MG corrèle significativement avec toutes les densités osseuses (DXA: r: -0.53 à -0.18) et tous les paramètres d'architecture osseuse [QPCT: indices de torsions/force (r=-0.44 à -0.28), densité corticale (r=-0.33) et de la moelle (r=+0.19)].

Conclusion: Utiliser des indicateurs cliniques reflétant l'adiposité semblent permettre de mieux identifier les aînés à risque de présenter des paramètres osseux moins favorables.

Mots clés : masse grasse, densité osseuse, architecture osseuse, vieillissement, ostéoporose

ABSTRACT

Introduction**:** Osteoporosis is an age-related condition that can lead to fragility fractures, morbidity, mortality, and societal consequences. One of the known risk factors for bone fragility is low body mass index (BMI). However, the impact of obesity on bone health is still subject to debate. One possible reason for this disparity is that BMI might be an imperfect marker of obesity in older adults. Thus, to help the clinician identify older adults at risk of fractures, other clinical markers of excess adipose tissue (such as the percentage fat mass (FM) or the waist circumference (WC)) should be assessed.

Aims: 1) To examine the relationship between bone parameters and three obesity criteria; (2) To compare bone parameters in obese vs. non-obese older adults.

Methodology: We performed a cross-sectional study of 145 sedentary people (91 men and 54 women) aged between 55 and 80 in the Montreal area of Québec, Canada. Participants were classified as obese or not, according to three clinical parameters: BMI (> 30 kg/m^2), WC (W>80 cm; M>94 cm) or FM (W>40%; M>27%). Body composition (fat, bone and lean density/quantity/quality) was assessed using dual-energy X-ray absorptiometry (DXA) or peripheral quantitative CT (pQCT).

Results: 145 people were included in the study: the number of obese people was 44 (30%) according to the BMI, 95 (65%) according to the FM, and 119 (82%) according to the WC. Patients who were obese according to the WC and FM had a less favourable bone profile than patients classified as non-obese. The opposite was true for people classified as obese according to the BMI. Only the FM was significantly correlated with all bone density variables (DXA; -0.53 to -0.18) and all bone architecture parameters [pQCT: force and strength indexes (Pearson correlation coefficient : r=-0.44 to -0.28), cortical density (r=-0.33) and marrow density (r =+0.19)].

Conclusion: Clinicians should use clinical indicators of adiposity to identify older adults at risk of having less heathy bone parameters.

Keywords: fat mass, bone density, bone architecture, aging, osteoporosis

INTRODUCTION

Osteoporosis is an age-related skeletal disease characterized by low bone mass and microarchitectural deterioration of the bone tissue, leading to bone fragility and fractures (WHO, 1994). The estimated prevalences of osteoporosis are respectively 15% and 30% in men and women over the age of 50 and 46% and 77% in men and women over the age of 80[1]. Given the many consequences of population ageing, osteoporosis is a major public health issue. Indeed, the number of fractures (including hip fractures) is expected to rise by 50% between 2000 and 2050 [2,3,4]. Furthermore, osteoporotic fracture increases the risk of death [5], loss of physical autonomy, and the likelihood of hospitalization. In Europe, the estimated economic burden of osteoporotic fracture is 37 billion euros per year[6].

Low bone mineral density (BMD) is the main factor directly and linearly associated with an increase in fracture risk[7]. However, low BMD does not fully account for the increase in the incidence of hip fracture with age[8]. In fact, factors not associated with age (e.g. biological sex) or weakly associated with age (e.g. nutrition (vitamin D/calcium deficiencies) and body composition (fat and muscle masses)) are also linked to the osteoporosis fracture risk[9].

However, the literature data on osteoporosis in obese patients is contradictory. For example, it has been reported that obesity protects against osteoporotic fracture [10] and a decrease in hip and spine BMD (i.e. osteoporosis status)[11]. Furthermore, a study of post-menopausal women showed that a higher body mass index (BMI) was associated with a higher BMD but lower indices of bone strength[12,13]. Bone strength and bone architecture are biomarkers of the fracture risk. Accordingly, it has been reported that obese people have a greater BMD and fewer osteoporotic fractures as a result of greater skeletal loading and tissue padding[14]. Nevertheless, other studies have come to the opposite conclusion. For example, it has been reported that obesity may increase the risk of fracture, due to (i) greater impact forces during a fall[12,15] and (ii) the secretion of pro-inflammatory cytokines that harm bone tissue[16]. Greater weight or fat mass (FM) is reportedly associated with fractures in women[12,17] and in men[18].

One explanation for the discrepancies in the literature data is that obese populations are phenotypically heterogeneous with regard to fat distribution (visceral vs. subcutaneous) and metabolic complications. Given that different types of fat (e.g. subcutaneous vs. visceral, or gynoid/appendicular vs. android) have different health consequences and that aging can cause a change in body composition without a change in body weight[19], the BMI might not be a perfect indicator of body fat[20]. Accordingly, waist circumference (WC, which reflects abdominal obesity[21]) is associated with an increased risk of hip fracture[22]. Furthermore, FM is considered to be better clinical marker of obesity than BMI in older adults[23], and similar results have been reported for a high FM and fracture risks[24]. Around 20% of obese people are metabolically healthy[25], whereas around 10% have a low muscle mass and low strength (referred to as “sarcopenic-obese”). Sarcopenic obesity is known to have an impact on bone health, such as an increased fracture risk in older men[26]. This finding is reinforced by the negative impact of sarcopenic obesity on bone mineral density[27,28]. One potential explanation for this relationship is that infiltration of fat into skeletal muscle is associated with an increased risk of hip fracture[29]; however, these conclusions regarding bone architecture are subject to debate[30].

Another possible explanation is that the BMD estimated with dual-energy X-ray absorptiometry (DXA) may not be the best predictor of bone fragility. Indeed, a study found that 60% of a cohort of obese women (defined by the BMI) with a trauma fracture had a normal BMD, as measured by DXA [31]. Changes in microarchitecture (as measured by peripheral quantitative computed tomography (pQCT) were found to be the best predictors of fracture[32]. Thus, estimating bone architecture with pQCT appears to be clinically relevant.

Despite osteoporosis's clear impact on mortality, morbidity, and healthcare costs, this disease is still under-diagnosed and under-treated[33]. Therefore, the accurate identification of individuals at risk should be useful – especially for obese older adults. Thus, the objectives of the present study were to assess the relationship between body composition and bone parameters and to compare bone parameters in obese vs. non-obese people (defined according to different clinical criteria).

MATERIAL AND METHODS

Design:

We performed a retrospective, cross-sectional study (secondary analysis). All procedures were approved by the research ethics board at the Université du Québec à Montréal (Montréal, Québec, Canada). All participants provided their written consent after having received information on the study's design, objectives, procedures, and associated risks.

Population:

Participants were recruited from the community via adverts (flyers) displayed in the Montréal area. The main inclusion criteria were (i) age 60 or over, (ii) low physical activity for the previous 6 months (less than 2 hours of structured exercise per week), (iii) stable body weight (± 2 kg) over the previous 6 months, (iv) no orthopaedic limitations, (v) no contraindications to physical activity (assessed using the Physical Activity Readiness Questionnaire[34]), (vi) the absence of menstruation for the previous 12 months (for women), (vii) non-smoker status, (viii) low alcohol consumption (≤2 alcoholic drinks/day) and, (iv) residence in the community. People with diagnosed and active neurological, cardiovascular or lung diseases or cognitive disorders were excluded. Participants with a BMI ≤ 19 kg/m² were excluded.

Obesity/group criteria:

Weight classes were defined using three validated clinical markers: BMI (according to the WHO[35]; the clinical gold standard), FM (expressed as a percentage of bodyweight)[23], and WC[36]. Obesity was variously defined as a BMI ≥30 kg/m² (according to the WHO[35]; the clinical gold standard), a total FM >28% for men and >40% for women[23], or a WC >94 cm for men and >80 cm for women[36]. People with a BMI <25 kg/m² were defined as non-obese, and people with a BMI between 25 and 30 were defined as overweight.

Data collection:

The data were collected by highly trained clinical evaluators at the university's Department of Exercise Science.

- Anthropometric characteristics:

Body weight (kg) and height (m) were determined in the fasting state using an electronic scale (Adam GFK 660a) and a stadiometer (Seca), and the BMI (body mass (kg)/height (m^2)) was calculated. Waist circumference was measured to the nearest 0.5 cm using a flexible but non-stretchable measuring tape, with the participant standing upright.

- Body composition

Total, android and gynoid FM (%), total and appendicular (leg+arm) lean mass (LM; kg), total, hip and spine bone mass density (BMD; g/cm^3) and arm and leg bone mineral content (BMC) were quantified by dual-energy X-ray absorptiometry (DXA; GE Medical Systems, Madison, WI, USA). Furthermore, osteoporosis status (bone fragility) was evaluated using T-score values at each site (total, hip, and spine). A T score of between +1 and -1 corresponded to normal bone mineral density, with a T-score of between -1 and -2.5 for osteopenia and a T-score of -2.5 or less for osteoporosis. For the evaluation of body composition, participants were asked to fast and to remove all jewellery prior to DXA. Scans were performed with the participant in the supine position.

- Bone architecture/bone quality

A peripheral quantitative computed tomography (pQCT) scan at a point one third of the way up the right femur (measured from the lateral epicondyle to the greater trochanter) was performed using a Stratec XCT3000 system (STRATEC Medizintechnik GmbH). The total femur length, voxel size (0.5 mm) and scan speed (10 mm.s^{-1}) were entered into the pQCT system's software. All scans were performed by operators trained in pQCT data acquisition according to the guidelines provided by Bone Diagnostics, Inc. (Fort Atkinson, WI, USA). After data acquisition, image quality was assessed visually by a second investigator. The visual inspection rating scale, performed by two different investigators (agreement between both investigators: 77%), classified all images as a rate up to 3 [37]. The pQCT density distribution plugin for ImageJ software (version 1.3.11) was used to analyze the images [38]. Results were provided automatically in the ImageJ analysis output. The thresholds for BMD, cortical density (mg/cm^3), and biomechanical indexes (the strength strain index (SSI, mm^3), the bone compressive strength index (BSI, g^2/cm^4) and two measures reflecting torsional bone strength (the polar second moment of area (IPo, mm^4) and density- weighted IPo (dwIPo, mg/cm)) were based on previously published values [38]. For determination of cortical bone geometry, the error ranges are reportedly between 2.1 for total aera and 3.7% for cortical aera.[39].

In order to characterize our participants and compare our results with the literature data, we also assessed physical performance and the level of physical activity.

- Physical performance

Maximal isometric lower limb muscle strength was assessed with a strain gauge system attached to a chair. The participant was seated with the hip-joint angle set to 90°.

Maximal isometric upper limb muscle strength was assessed using a handheld dynamometer with an adjustable grip (Lafayette Instrument Co., Lafayette, IN, USA). Participants were asked to squeeze the dynamometer as hard as possible for 4 s in a standing position, with the arms alongside the body. Three measurements for each hand were recorded alternately, and the best score was selected for analysis. Low muscle strength was defined as a value below 16 kg in women and below 27 kg in men; this corresponds to probable sarcopenia[40].

Gait parameters: in order to evaluate gait velocity, the 3-meter "timed up and go" (TUG) test (unit: seconds) was performed at a comfortable, self-paced speed [41]. The TUG test result is known to be associated with the risk of falls.

Mobility in the 6-minute walking test (6MWT): participants were instructed to walk as far as possible during a 6-minute period. They received the same standardized encouragement every minute and were allowed to slow down or stop at any time. The 6MWT is a validated test for assessing mobility[42].

- *Level of physical activity:*

The number of steps was estimated using a validated triaxial accelerometer (SenseWear® Mini Armband), as described by Colbert et al.[43]. For 7 consecutive days, participants had to wear the device on their left arm at least 85% of the time (i.e. except when taking a shower or swimming).

Statistical analyses:

Baseline characteristics were summarized using descriptive statistics. Continuous variables were quoted as the mean ± standard deviation (SD). A T-test was used to compare non-obese and obese groups with regard to bone parameters, body composition, and functional capacities. Pearson's coefficient was calculated for correlations between adipose markers (BMI, FM, or WC) and bone parameters. Sub-analyses were performed by sex. For each obesity measure, subgroup analyses were performed on the corresponding obese group only. Given that muscle endurance (e.g. 6MWT distance) and grip strength are known to influence bone parameters, our statistical analyses included these factors as covariables. All statistical analyses were performed with SPSS for Windows software (version 27.0, IBM Corp., Armonk, NY, USA). The threshold for statistical significance was set to $p<0.05$.

RESULTS

A total of 144 participants were included in this cross-sectional study. The participants' main characteristics are summarized in Table 1. The mean age was 67 ± 5, the majority (62.5%) of the participants were men, and 55 participants (38%) were considered to have bone fragility (osteoporosis or osteopenia, according to the WHO Z-score obtained using DXA). Although 52 (36%) participants were classified as non-obese according to the BMI (BMI < 30 kg/m2), they presented a high FM (mean ± SD: 35.3 ± 8.3%). Furthermore, the mean android and gynoid FM mass contents were 44.7% ± 8.3% and 36.7% ±10.4%, respectively. The proportion of obese participants depending on the obesity criterion used: 30% (n=44) according to the BMI (forming the "obese-BMI" group), 65% (n=95) according to the FM (the "obese-FM" group), and 82% (n=119) according to the WC (the "obese-WC" group).

<u>Relationship between body composition and bone parameters:</u>

The correlations between BMI, total BMD, total T-score and cortical density were statistically significant (p<0.05) but weak (r<0.3) (Table 2).

In the obese-BMI group, only cortical density was negatively correlated with BMI (r= -0.354, p=0.003; Supplemental Table). Waist circumference was correlated with SSI, dwIPo and IPo (r=0.199, p=0.017; r=0.217, p=0.017; and r=0.250, p=0.003, respectively) and total BMD (r=0.310, p< 0.001). The same correlations were found for WC and bone parameters in the obese-WC group (n=119), except that WC and cortical density were not correlated (r=-0.121, p=0.91, Supplemental Table).

The FM was the only obesity criterion that was significantly correlated with all the bone parameters (density, quality, and composition). For example, FM was negatively correlated with arm or leg BMC as estimated using DXA (r=-0.529, p< 0.001; and r=-0.441, p<0.001, respectively). FM was correlated also with all bone density variables, such as bone cortex or marrow density estimated using pQCT (cortex: r=-0.248; p<0.05; marrow: r=0.186; p=0.026). Lastly, FM was negatively and moderately correlated with the biomechanical indexes (SSI: r =-0.436, p < 0.001; BSI: r= -0.28, dwIPo: r=-0.386; IPo: r=-0.346; p<0.001). The same correlations were found for between FM and bone parameters in the obese-FM group (n=95; Supplemental Table).

Cortical density was the only bone parameter that was significantly correlated with all three obesity measures (BMI: r=0.218; WC: r= -0.234; FM: r=-0.329). Similar results were observed after correction for grip strength and the 6MWT distance (Supplemental Table).

Sub-analyses did not reveal any correlations between bone parameters (DXA) in men only (n=91; Supplemental Table), except for spine BMD and FM (r=-0.224, p=0.036). As in the analyses of the overall study population, the cortical density was negatively correlated with all three obesity measures (Supplemental Table). For the biomechanical indexes, dwIPo and IPo were positively correlated with the BMI but all other relationships were not significant (Supplemental Table). A subanalysis of women only (n=54) gave different results. Firstly, spine and hip BMD were positively correlated with BMI and WC (Supplemental Table). Cortical density was correlated with BMI (r=-0.288, p=0.035) but not with WC or FM. SSI, dwIPo and IPo were correlated with WC (SSI: r=0.271; p= 0.050, dwIPo: r=0.319, p=0.02; IPo: r=0.373, p=0.006). However, there were no significant correlations between FM and bone parameters when considering all the women only (Supplemental Table).

Comparison between obese and non-obese groups:

- *Obese/non-obese groups, as defined with the BMI (Table 3)*

BMD and BMC values were significantly higher in overweight participants than in normal-weight participants, as observed for the total BMD (1.23 vs. 1.12 g/cm²), hip BMD (1.04 vs. 0.96 g/cm²), arm BMC (0.41 vs. 0.32 g, respectively) and leg (1.18 vs. 1.0 g, respectively) BMC (see Table 3; $p<0.05$). The same was true for the strength indexes (SSI: 3164 mm^3 in overweight participants vs. 2698 in non-obese participants; dwIPo: 6403 vs. 5202 mg/cm; BSI: 3.38 vs. 2.85 g^2/cm^4,; IPo: 59652 vs. 48632 mm^4, respectively) (Table 3; $p<0.05$). Arm BMC was significantly lower in obese participants than in overweight participants (0.41 vs. 0.37 g,; $p=0.047$).

- *Obese/non-obese groups, as defined with the FM (Table 4)*

There were no differences in bone parameters between obese and non-obese groups defined with the FM. Only total BMD and hip BMD were slightly and non-significantly higher in obese participants compared to non-obese participants (1.22 vs. 1.18 g/cm²; $p=0.054$ and 1.036 vs. 0.988 g/cm², $p=0.063$ respectively).

- *Obese/non-obese groups, as defined with the WC (Table 5)*

Hip BMD (1.008 vs. 1.085 g/cm²; $p=0.018$), arm (0.36 vs. 0.44 g; $p=0.001$) and leg (1.1 vs. 1.2 g; $p=0.0018$) BMC were lower in obese participants than in non-obese participants. Regarding bone parameters estimated using pQCT, cortical density (1092 in obese participants vs. 1111 mg/cm^3 in non-obese participants; $p=0.009$), SSI (2974 vs. 3393 mm^3, ;$p=0.007$), IPo (55894 vs. 65114 mm^4,; $p=0.011$) and dwIPo (55894 vs. 64625 mg/cm; $p=0.005$) were lower in obese participants than in non-obese participants.

DISCUSSION

The present study compared bone parameters in obese and non-obese people defined by various criteria and assessed the relationships between these parameters.

Firstly, healthy bone parameters were positively associated with the BMI but a high WC or a high FM were rather associated with unfavourable parameters. Furthermore, we observed that overweight older adults also tended to have healthier bone parameters. This observation is in line with Kim et al.'s report of a nonlinear association between BMI and hip fracture and a low bone fracture risk in overweight participants[44]. Furthermore, about a third of participants in the present study had a high FM but were not obese, according to the BMI. In Scott et al.'s study, high-FM, BMI-obese participants had a higher osteoporosis risk than all other participants [45]. Thus, our results suggest that a high FM (reflecting obesity) is associated with less favourable bone parameters. This result is supported by similar results in the literature. For example, Kim et al. observed a negative association between FM and BMC, after adjustment for age and weight [46]. Furthermore, it has been observed that visceral FM (estimated by DXA) was negatively correlated with BMD (R=-0.368, p=0.017) after controlling for BMI in postmenopausal women [47]. Similar results have been found with regard to the use of WC to define obesity. For example, a meta-analysis showed that having a high WC increased the risk of hip fracture by a factor of 1.58 [95% CI: 1.20-2.08], relative to people with a lower WC [22].

Sex differences in bone variables have also been well documented. The bone turnover induced by the menopause means that women have a higher risk of osteoporosis and fracture than men [48], although the gap narrows with age[49]. Thus, bone mass is higher in men than in women but the BMD is similar[50]. The estimated fracture risk as a function of BMD is the same in men and women[49,51]. However, it has been suggested that women present a greater decrease in cortical BMD (25%, vs. 18% in men; p<0.001) and trabecular BMD (55% vs. 46%, respectively; p<0.001) with age[52]. Furthermore, bone strength falls more quickly with age in women than in men[53]. In the present study, cortical density was negatively correlated with all measurements in obese women only, which is consistent with the data cited above. It is not clear whether the effect of obesity on bone depends on sex. Some studies did not find a sex difference[54], whereas some others showed that the correlation between FM and BMD was stronger in women than in men [55,56].

There are several physiopathologic explanations for the harmful impact of obesity on bone. First, obesity is known to induce systemic inflammation, with greater secretion of proinflammatory cytokines like tumour necrosis factor alpha and interleukin-6. Proinflammatory cytokines stimulate bone resorption and lead to bone loss in the long term[16]. Moreover, the chronic low-grade inflammation observed with age – the so-called "inflammaging" – is thought to have a role in age-related diseases[57], although this has not yet been proven for osteoporosis [58]. Vitamin D deficiency is more prevalent (by around 35 percentage points) in obese populations than in non-obese populations [59]. The major suspected mechanism affecting bone is the sequestration of vitamin D (as a lipophilic vitamin) in adipose tissue. It has been hypothesized that obesity increases the fat content of the bone marrow[60] and that fat accumulation in the bone marrow is increasingly prevalent with age[61].

In the present study, the three obesity criteria were correlated with cortical density – suggesting that the latter parameter is strongly related to obesity and not dependent to obesity measurement criteria. This finding is important because cortical BMD in the tibia is low in obese populations and related to the severity and/or number of fractures [32,62]. Furthermore, it is well known that bone parameters estimated using pQCT are more strongly related to osteoporosis and the fracture risk than bone density parameters estimated using DXA[31],[63,64]. According to the literature, cortical indexes appear to predict the response to antiresorptive treatments in osteoporosis[65]. At present, pQCT is mostly a research tool capable of identifying bone alterations not detected with DXA. Thus, pQCT should be considered as an important decision-support tool because it enables the physician to obtain a detail view of overall bone health in specific, at-risk populations such as that studied here. Moreover, an association between FM and alterations in pQCT parameters has been detected in childhood [66], middle age [67], and in patients with comorbidities (such as those on peritoneal dialysis) [68]. Thus, given that FM is the only obesity criterion correlate with all bone parameters at all bone sites, we suggest that this criterion should be used by the physician to identify obese older adults at risk of bone fracture. However, it is important to note that according to the literature, LM is a better predictor of bone health than FM [69,70] . Hence, the physician should consider identifying older adults with obesity and a sarcopenia phenotype because the sarcopenia-obesity combination appears to increase the likelihood of bone fragility. Our results and the literature data[22] suggest that WC (i) is a good alternative if DXA cannot be used or is not available and (ii) can be used to easily evaluate bone changes in obese older adults in routine clinical practice.

The present study also had some limitations. First, the study's cross-sectional design prevents us from identifying causal relationships. Secondly, the nature of our study sample limits the external validity of our results. Compared with older adults in the general population, our participants were in good health (due to our selection criteria), which prevents us from generalizing our results to the older population. However, the prevalence of weak grip strength in our study was similar to that observed in the community [71]. Thirdly, the large number of bivariable comparisons performed means that there is a risk of false positives. Fourthly, the retrospective design meant that we did not have data for certain confounding factors, such as prior fractures, weight history or menopausal history; this also limited the external validity of our results. However, the present study also had a number of strengths. Firstly, we estimated bone parameters (density and architecture) using gold-standard techniques (pQCT and DXA). Secondly, we included both men and women and so could assess putative sex differences. Lastly, the present study was one of the first to compare three clinical validated markers of obesity.

In conclusion, clinical indicators of adiposity other than BMI might help health professionals to (i) identify older adults with poor bone health or an elevated risk of osteoporosis fracture and therefore (ii) suggest clinical interventions for preventing bone-related consequences, such as fall fractures and loss of mobility.

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TABLES

Table 1. Main characteristics of the study participants (n=144)

Variable	Participants
GENERAL CHARACTERISTICS	
Age (years)	67 ± 4.9
Female (n)	54 ± 37.5
WC (cm)	102 ± 12.4
Prevalence of obesity, according to the WC (n)	119 (82%)
BMI (kg/m^2)	28.6 ± 4.8
Prevalence of obesity, according to the BMI (n)	44 (30%)
BODY COMPOSITION (DXA)	
Total LM (kg)	49 ± 9.6
Appendicular LM (kg)	23 ± 4.9
Total FM	35.3 ± 8.7
Prevalence of obesity, according to the FM (n)	95 (65%)
Android FM	44.7 ± 8.3
Gynoid FM	36.7 ± 10.4
Total BMD (g/cm^2)	1.205 ± 0.12
Spine BMD (g/cm^2)	1.192 ± 0.21 *
hip BMD (g/cm^2)	1.020 ± 0.12 *
Total T-score	0.166 ± 1.2 ***
Spine T-score	-0.006 ± 1.6 ***
Hip T-score	-0.326 ± 1.04***
Arm BMC (g)	0.38 ± 0.11
Leg BMC (g)	1.124 ± 0.21
Prevalence of osteopenia/osteoporosis (n)	55 (38%) *
BONE PARAMETERS (pQCT)	
BMD (g/cm^2)	1.1 ± 0.03
Cortical density (mg/cm^3)	1096 ± 32
SSI (mm^3)	3046 ± 706
IPo (mm^4)	57 505 ± 16500
dwIPo (mg/cm)	6140 ± 1792
BSI (g^2/cm4)	3.24 ± 0.76
PHYISCAL PERFORMANCE	
grip strength (kg)	35 ± 10
Weak grip strength (n)	13 (9%)
LLMS (kg)	292 ± 158
6MWT distance (m)	572 ± 89.5
Normal 3-metre TUG (s)	10 1.6
LEVEL OF PHYSICAL ACTIVITY	
Number of steps (n)	6950 (3233)

*Legends: Data are quoted as the mean ± SD or n (%). Number of participants included: * (n=142); ** (n=127); *** (n=117). WC=waist circumference; BMI= bone mass density. Appendicular=arm + leg;*

BMD: bone mass density; BMC: bone mineral content;LM=lean mass; FM=fat mass; SSI= strength strain index, BSI=compressive strength index; IPo= polar second moment of aera; DwIPo= density-weighted polar second moment of area LLMS= lower limb muscle strength; 6MWT: *mobility in the 6-minute walking test, TUG = timed up and go test*

Table 2. Correlations between obesity criteria, bone parameters, and body composition (n=144)

Variable	BMI	WC	FM
BMI (kg/m²)	1	0.810 (0.744;0.859) *	0.670 (0.567;0.750) *
WC (cm)	0.465 (0.324; 0.583) *	1	0.465 (0.324; 0.583) *
BODY COMPOSITION (DXA)			
Total FM	0.670 (0.567; 0.750) *	0.465 (0.324; 0.583) *	1
Android FM	0.629 (0.517; 0.718) *	0.597 (0.478; 0.692) *	0.813 (0.747; 0.861) *
Gynoid FM	0.365 (0.214; 0.498) *	0.157 (-0.008; 0.313)	0.854 (0.802; 0.893) *
Total LM (kg)	0.336 (0.182; 0.474) *	0.458 (0.318; 0.579) *	-0.343 (-0.480; -0.190) *
Appendicular LM (kg)	0.169 (0.005; 0.324) *	0.307 (0.150; 0.449) *	-0.469 (-0.588; -0.330) *
Total BMD (g/cm²)	0.235 (0.073; 0.384) *	0.310 (0.152; 0.451) *	-0.212 (-0.363; -0.049) *
Spine BMD (g/cm²)	0.096 (-0.071; 0.256)	0.132 (-0.035; 0.290)	-0.248 (-0.396; -0.086) *
Hip BMD (g/cm²)	0.159 (-0.007; 0.315)	0.191 (0.026; 0.345) *	-0.176 (-0.330; -0.011) *
Arm BMC (g)	-0.042 (-0.205; 0.123)	0.121(-0.046; 0.280)	-0.529 (-0.637; -0.297) *
Leg BMC (g)	0.076 (-0.120; 0.206)	0.289 (0.022; 0.339) *	-0.441 (-0 .563; -0.297) *
Spine T score	0.100 (-0.084; 0.276)	0.151 (-0.032; 0.323)	-0.177 (-0.347; 0.005)
Hip T score	0.100 (-0.083; 0.276)	0.112 (-0.072; 0.287)	-0.081 (-0.258; 0.103)
Total T score	0.218 (0.038; 0.383) *	0.266 (0.089; 0.426) *	-0.053 (-0.232; 0.129)
BONE PARAMETERS (pQCT)			
marrow density (g/cm²)	0.109 (-0.056; 0.267)	-0.013 (-0.177; 0.151)	0.186 (0.022; 0.338) *
Cortical density (mg/cm³)	-0.271 (-0.416; -0.112) *	-0.234 (-0.383; -0.072) *	-0.329 (-0.467; -0.174) *
SSI (mm³)	0.066 (-0.098; 0.227)	0.199 (-0.396; -0.086) *	-0.436 (-0.559; -0.292) *
dwIPo (mg/cm)	0.112 (-0.054; 0.271)	0.217 (0.035; 0.351) *	-0.386 (-0.516; -0.235) *
IPo (mm⁴)	0.148 (-0.017; 0.305)	0.250 (0.089; 0.398) *	-0.346 (-0.482; -0.192) *
BSI (g²/cm4)	0.045 (-0.120; 0.207)	0.077 (-0.089; 0.238)	-0.280 (-0.423; -0.121) *
PHYSICAL PERFORMANCE			
GRIP STRENGTH (kg)	-0.074 (-0.235; 0.091)	0.062 (-0.104; 0.223)	-0.335 (-0.472; -0.180) *
LLMS (kg)	-0.045 (-0.227; 0.140)	0.064 (-0.121; 0.245)	-0.319 (-0.474; -0.142) *
6MWT (m)	-0.225 (-0.374; -0.063) *	-0.229 (-0.378; -0.066) *	-0.361 (-0.494; -0.208) *
Normal TUG (s)	0.151 (-0.013; 0.307)	0.101 (-0.064; 0.261)	0.128 (-0.037; 0.285)
LEVEL OF PHYSICAL ACTIVITY			
Steps per day (n)	-0.242 (-0.374; -0.063) *	-0.222 (-0.382; -0.048) *	-0.229 (-0.387; -0.056) *

Legends: comparisons were performed using Pearson's correlation test. * $p < 0.05$. *WC=waist circumference; BMI= bone mass density. Appendicular=arm + leg; BMD: bone mass density ; BMC: bone mineral content; LM=lean mass; FM=fat mass, SSI= strength strain index, BSI=compressive strength index; IPo= polar second moment of aera; DwIPo= density-weighted polar second moment of area; ULMS=upper limb muscle strength; LLMS= lower limb muscle strength;* 6MWT: m*obility in the 6-minute walking test, TUG = timed up and go test*

Table 3. Comparison of physical parameters in obese, overweight vs. non-obese groups, defined according to the BMI.

Variable	**Non obese (n=32)**	**overweight (n=69)**	**Obese (n= 44)**
Age (years)	67 (5.5)	68 (4.7)	67 (4.5)
WC (cm)	87 (6.3)	102* (6.7)	113 (11.4) *+
BMI (kg/m2)	23 (1.6)	27* (1.4)	34 (4) *+
BODY COMPOSITION (DXA)			
Total FM	29 (8.5)	33 (6.4) *	42(6.9) *+
Android FM	37 (9.6)	45 (6.2) *	51(5.2) *+
Gynoid FM	35 (11.2)	34 (9.4)	42(9.2) *+
Total LM (kg)	42 (7.8)	50.1 (8.8) *	52.9 (9.6)
Appendicular LM (kg)	19.7 (4.2)	24.0 (4.6) *	23.9 (4.8) *
Total BMD (g/cm^2)	1.124 (0.10)	1.229 (0.11) *	1.226 (0.11) *
Spine BMD (g/cm^2)	1.163 (0.23)	1.207 (0.21)	1.187 (0.19)
Hip BMD (g/cm^2)	0.955(0.13)	1.037 (0.15) *	1.044 (0.15) *
Arm BMC(g)	0.32 (0.1)	0.41 (0.1) *	0.37 (0.2) *+
Leg BMC (g)	0.1 (1.12)	1.18 (1.13) *	1.13(1.12) *
Spine T-score	-0.521 (1.84)	0.307 (1.64) *	-0.100 (1.32)
Hip T-score	-0.700 (0.96)	-0.180 (1.08) *	-0.255 (0.99)
Total T-score	-0.596 (1.13)	0.452 (1.15) *	0.324 (1.15) *
BONE PARAMETERS (pQCT)			
BMD (g/cm^2)	1.09 (0.02)	1.09 (0.03)	1.1 (0.03)
Cortical density (mg/cm^3)	1098 (35)	1100 (28)	1086 (34)
SSI (mm^3)	2698 (657)	3164 (682) *	3107 (713) *
Ipo (mm^4)	48 632 (14 605)	59 652 (16 197) *	60 440 (16 580) *
dwIPo (mg/cm)	5202 (1573)	6403 (1747) *	6394 (1819) *
BSI (g^2/cm4)	2.845 (0.64)	3.38 (0.72) *	3.3 (0.82) *
PHYSICAL PERFORMANCE			
GRIP STRENGTH (kg)	33 (10)	36 (10)	35 (11)
LLMS (kg)	272 (135)	310 (173)	276 (147)
6MWT (m)	563 (93)	593 (83)	547 (91) +
Normal TUG (sec)	9.99 (1.9)	9.87 (1.55)	10.19 (1.49)
PHYSICAL ACTIVTY LEVEL			
Steps/day (n)	8006 (3173)	7066 (3331)	6015 (2920)

Legends: comparisons were performed using a t- test. *Significant difference vs. the non-obese group ($P < 0.05$); + Significant difference vs. the overweight group ($P < 0.05$). *WC=waist circumference; BMI=bone mass density. Appendicular=arm + leg; BMD: bone mass density ; BMC: bone mineral content; LM=lean mass; FM=fat mass SSI= strength strain index, BSI=compressive strength index; IPo=polar second moment of area; DwIPo= density-weighted polar second moment of area, ULMS=upper limb muscle strength; LLMS=lower limb muscle strength;* 6MWT: m*obility in the 6-minute walking test, TUG = timed up and go test*

Table 4: Comparison of physical parameters in obese vs. non-obese people, defined according to the FM.

Variable	Obese (n= 95)	Non-obese (n=50)	p-value
Age (years)	67 (5.3)	67 (4.7)	0.72
WC (cm)	107 (11)	92 (9)	0.001
BMI (kg/m^2)	30 (2.8	25 (4.6)	0.001
BODY COMPOSITION (DXA)			
Total FM	38 (7.3)	29 (8.4)	0.001
Android FM	48 (5)	38 (8)	< 0.001
Gynoid FM	39 (10)	33 (11)	< 0.001
Total LM (kg)	50.2 (9)	47.3 (10.5)	0.102
Appendicular LM (kg)	23.3 (4.2)	22.5 (5.5)	0.375
Total BMD (g/cm^2)	1.219 (0.1)	1.178 (0.13)	0.054
Spine BMD (g/cm^2)	1.187 (0.19)	1.120 (0.24)	0.64
Hip BMD (g/cm^2)	1.036 (0.14)	0.988 (0.16)	0.063
Arm BMC (g/cm^2)	0.39 (0.1)	0.36 (0.12)	0.19
Leg BMC (g/cm^2)	1.15 (0.19)	1.08 (0.24)	0.1
Spine T-score	-0.025 (1.4)	0.025 (2)	0.96
Hip T-score	-0.263 (0.98)	-0.430 (1.15)	0.3
Total T-score	0.261 (1.13)	-0.040 (1.34)	0.21
BONE PARAMETERS (pQCT)			
BMD (g/cm^2)	1.1 (0.03)	1.09 (0.02)	0.19
Cortical density (mg/cm^3)	1093 (30)	1101 (34)	0.18
SSI (mm^3)	3107 (664)	2925 (768)	0.14
Ipo (mm^4)	59 290 (15 580)	53 940 (17 889)	0.070
dwIPo (mg/cm)	6316 (1693)	5789 (1922)	0.09
BSI (g^2/cm4)	3.31 (0.73)	3.10 (0.8)	0.11
PHYSICAL PERFORMANCE			
GRIP STRENGTH (kg)	35.6 (9.9)	34.9 (10.8)	0.7
LLMS (kg)	282 (158)	312 (157)	0.33
6MWT (m)	580 (90)	568 (88)	0.42
Normal TUG (s)	9.88 (1.47)	10.2 (1.88)	0.26
LEVEL OF PHYSICAL ACTIVITY			
Steps/ day (n)	6741 (3421)	7346 (2839)	0.32

Legends: comparisons were performed using a t- test. Significant difference: $p < 0.05$; *WC=waist circumference; BMI= bone mass density. Appendicular=arm + leg; BMD: bone mass density ; BMC: bone mineral content; LM=lean mass; FM=fat mass; SSI= strength strain index, BSI=compressive strength index; IPo= polar second moment of aera; DwIPo= density-weighted polar second moment of area; ULMS=upper limb muscle strength; LLMS= lower limb muscle strength;* 6MWT: m*obility in the 6-minute walking test, TUG = timed up and go test*

Table 5: Comparison of physical parameters in obese vs. non-obese groups, defined according to the WC.

Variable	Obese (n= 119)	Non-obese (n=25)	p-value
Age (years)	68 (5)	66 (5)	0.149
WC (cm)	104 (11)	91 (13)	0.001
BMI (mg/m²)	29 (5)	26 (5)	0.005
Total FM	37 (8)	28 (9)	0.001
Android FM	46 (7)	37 (9)	<0.001
Gynoid FM	38 (10)	29 (7)	<0.001
Total LM (kg)	48.4 (9.8)	52.9 (7.8)	0.018
Appendicular LM (kg)	22.6 (4.9)	25.4 (3.9)	0.003
Total BMD (g/cm²)	1.198 (0.12)	1.232 (0.11)	0.176
Spine BMD (g/cm²)	1.183 (0.21)	1.240 (0.19)	0.296
Hip BMD (g/cm²)	1.008 (0.14)	1.085 (0.14)	0.018
Arm BMC (g)	0.36 (0.11)	0.44 (0.08)	<0.001
Leg BMC (g)	1.1 (0.21)	1.2 (0.19)	0.011
Spine T score	0.022 (1.64)	-0.214 (1.60)	0.612
Hip T score	-0.341 (1.03)	-0.353 (1.14)	0.671
Total T score	0.219 (1.17)	-0.294 (1.48)	0.118
BONE PARAMETERS (pQCT)			
BMD (g/cm²)	1.10 (0.03)	1.1 (0.02)	0.76
Cortical density (mg/cm³)	1092 (31)	1111 (30)	0.009
SSI (mm³)	2974 (692)	3393 (683)	0.007
IPo (mm⁴)	55 894 (16 159)	65 114 (16 614)	0.011
dwIPo (mg/cm)	55894 (1740)	64624 (1781)	0.005
BSI (g²/cm4)	3.2 (0.7)	3.5 (0.8)	0.050
PHYSICAL PERFORMANCE			
GRIP STRENGTH (kg)	34 (10)	40 (8)	0.004
LLMS (kg)	309 (145)	228 (188)	0.059
6MWT (m)	558 (83)	639 (90)	<0.001
Normal TUG (s)	10.1 (1.65)	9.4 (1.32)	0.048
LEVEL OF PHYSICAL ACTIVITY			
Steps per day (n)	6795 (3123)	7693 (3701)	0.238

Legends: comparisons were performed using a t- test. Significant difference: $p < 0.05$; *WC=waist circumference; BMI= bone mass density. Appendicular=arm + leg; BMD: bone mass density ; BMC: bone mineral content; LM=lean mass; FM=fat mass SSI= strength strain index, BSI=compressive strength index; IPo= polar second moment of aera; DwIPo= density-weighted polar second moment of area; LLMS= lower limb muscle strength;* 6MWT: m*obility in the 6-minute walking test, TUG = timed up and go test*

Vu, le Directeur de Thèse

Mylene Aubertin-Leheudre
À Montréal, Le 19 septembre 2021

Vu, le Doyen
De la Faculté de Médecine de Tours
Tours, le

Lemoine Léa - 34 pages – 5 tableaux

Résumé :

Introduction : L'ostéoporose, est une condition liée à l'âge conduisant aux fractures de fragilité avec des conséquences en termes de morbidité, mortalité et sociétale. Même si avoir un faible IMC est un facteur de risque reconnu de fragilité osseuse, l'impact de l'obésité sur l'os (densité et architecture) est, elle contradictoire. Une des raisons possibles serait que l'IMC qui définit l'obésité est avec l'âge un marqueur imparfait. Ainsi, d'autres marqueurs cliniques du tissu adipeux (pourcentage de masse grasse (MG) ou tour de taille (TT)) devraient être explorés.

Objectif : 1) Examiner la corrélation entre les différentes mesures d'obésités et les paramètres osseux; 2) Comparer les paramètres osseux entre des aînés obèses et non-obèses selon 3 critères d'obésité

Méthodologie : Étude transversale incluant 145 hommes (H; n=91) et femmes (F; n=54) âgés de 55 à 80 ans, sédentaires et habitants au Québec (Canada). Les participants ont été classés obèses ou non selon 3 paramètres: l'IMC (>30kg/m^2), le TT (F>80cm; H>94cm) et le pourcentage de MG (F>40%; H>27%). La composition corporelle (grasse, osseuse et musculaire) ont été recueillis via un ostéodensitométrie (DXA) et un CT-scan périphérique (QPCT; XCT-3000).

Résultats : Parmi les 145 sujets inclus, 44 étaient obèses selon l'IMC, 95 selon le pourcentage de MG et 119 selon le TT. Les patients obèses selon le TT et le % MG avaient des paramètres osseux moins favorables que ceux non-obèses. Par contre, cette observation était inversée pour ceux classés obèses selon l'IMC. Au niveau des corrélations, seul le % de MG corrèle significativement avec toutes les densités osseuses (DXA; r: -0,53 à -0,18) et tous les paramètres d'architecture osseuse [QPCT; indices de torsions/force (r=-0,44 à -0,28), densité corticale (r=-0,33) et de la moelle (r=+0,19)].

Conclusion : Utiliser des indicateurs cliniques reflétant l'adiposité semblent permettre de mieux identifier les aînés à risque de présenter des paramètres osseux moins favorables.

Mots clés : masse grasse, densité osseuse, architecture osseuse, vieillissement, ostéoporose

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