Année 2022/2023 N°

Thèse

Pour le

DOCTORAT EN MEDECINE

Diplôme d'État

Par

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Née le 23 mai 1996 à Paris 15ème (75)

Lien muscle-os : relation entre données musculaires et microarchitecture osseuse

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Présentée et soutenue publiquement le 16 octobre 2023 devant un jury composé de :

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Abstract in French / Résumé en français :

Abréviations : DMO = densité minérale osseuse, IMC = body mass index, BSI = indice de déformation osseuse, DEXA = absorptiométrie biphotonique à rayons X, HR-pQCT = tomodensitométrie périphérique quantitative à haute résolution, SSI = index de résistance osseuse.

Introduction : L'ostéoporose et la sarcopénie sont des conditions liées à l'âge, partageant des caractéristiques communes, et augmentant respectivement le risque fracturaire et le déclin des capacités physiques. L'étude osseuse tridimensionnelle permet l'analyse quantitative et qualitative de la microarchitecture osseuse et prédit avec plus de précision le risque de fracture de fragilité que la technique de référence (absorptiométrie biphotonique à rayons X, DEXA).

Objectif : L'objectif de l'étude était d'étudier la relation entre des données musculaires et la microarchitecture osseuse évaluée par un microscanner osseux et de déterminer quelle variable musculaire était la plus prédictive des paramètres de microarchitecture osseuse.

Méthodologie : Nous avons réalisé une étude transversale, incluant des participants, âgés de 60 à 81 ans, sédentaires, vivant dans la communauté de Montréal au Québec. Les paramètres musculaires et osseux ont été recueillis par DEXA et microscanner osseux de haute résolution (densité et aire corticale, densité et aire trabéculaire, index biomécanique). Plusieurs tests fonctionnels utilisés en pratique clinique ont également été collectés pour étudier les performances physiques. Il a été réalisé des corrélations ajustées sur le sexe et l'âge et une régression linéaire à partir des corrélations statistiquement significatives.

Résultats : 146 participants ont été inclus. Parmi les participants, 37% (n= 54) présentaient une ostéopénie et 4% (uniquement des hommes) présentaient une ostéoporose vertébrale selon le T-score en DEXA. 23% des participants (n = 35) étaient considérés comme sarcopéniques.
Des corrélations positives étaient retrouvées entre la masse maigre totale et appendiculaire et les paramètres osseux évalués en HR-pQCT. Il a été mis en évidence que la masse maigre appendiculaire était le facteur le plus prédictif concernant l'aire corticale ($R = 0,600$, $p < 0,001$), mais également des index de contrainte osseuse (SSI : $R = 0,550$, $p < 0,001$, BSI : $R = 0,491$, $p < 0,001$). La masse maigre totale était le paramètre le plus prédictif concernant l'aire osseuse totale ($R = 0,535$, $p < 0,001$) et l'aire trabéculaire ($R = 0,362$, $p < 0,001$).

Conclusion : Dans une population québécoise d'âge moyen, la plupart des paramètres musculaires et fonctionnels semblent liés à la microarchitecture osseuse. Cependant, la masse maigre est le facteur le plus prédictif et donc un indicateur pertinent à utiliser dans l'étude de la relation muscle-os.

Muscle-bone link: relationship between muscle data and bone microarchitecture

Abbreviations: BMD = bone mineral density, BMI = body mass index, BSI = bone strain index, DEXA = dual energy X-ray absorptiometry, EWGSOP2 = European Working Group of Sarcopenia in Older People 2, HR-pQCT = high-resolution quantitative peripheral computed tomography, SSI = strength strain index

Abstract in English:

Introduction:
Osteoporosis and sarcopenia are age-related conditions sharing common characteristics, increasing respectively fragility fracture risk and physical disability.
Three-dimensional bone analysis methods, such as quantitative peripheral CT-scan could be used to analyse alteration of the bone microarchitecture and to predict more precisely the bone fracture risk than dual energy X-ray absorptiometry (DEXA), which remains the gold standard.

Aim of the study: the aim of the study was to determine the association between muscle compartment parameters and bone microarchitecture assessed by quantitative peripheral CT-scan and to determine which muscle parameter was the most predictive of the bone compartment.

Methodology: We designed a cross-sectional study including 146 voluntary participants, aged between 60 and 81 years, sedentary, living in the community in Montreal area (Quebec, Canada). Body composition was described using DEXA. Bone microarchitecture parameters were assessed high resolution quantitative peripheral CT-scan (QPCT; XCT-3000). Clinical functional tests were collected to study physical performance. Sex and age- adjusted correlations were used followed by linear regressions on significant correlations.

Results: Among the participants included, 37% (n = 54) presented osteopenia and 4% (men only) presented vertebral osteoporosis according to the DEXA T-score. 23% of participants (n = 35) were considered sarcopenic. Concerning physical performance, better scores for the chair stand test and the handgrip test were found among men. Positive correlations were also detected between total/appendicular lean mass and bone parameters in bone microarchitecture.
Appendicular lean mass index was identified in regression as the strongest positive influencing factor on altered cortical area ($R = 0,600$, $p < 0,001$) but also on strain bone indexes (SSI: $R = 0,550$, $p < 0,001$, BSI: $R = 0,491$, $p < 0,001$). Also, total lean body mass index influenced positively and strongly total bone area ($R = 0,535$, $p < 0,001$) and trabecular area ($R = 0,362$, $p < 0,001$).

Conclusion:
In a young older Quebec population, most muscular and functional parameters appear to be linked to bone microarchitecture. A low lean mass was the best predicting muscular factor on altered bone microarchitecture evaluated by HR-pQCT.

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A Monsieur le Professeur Bertrand FOUGERE,
Pour l'honneur que vous me faites de présider ce jury et pour votre investissement dans l'enseignement de la gériatrie tout au long de mon internat.

A Madame le Docteur Léa LEMOINE,
Pour l'honneur que tu m'as fait en acceptant de diriger cette thèse. Pour ta gentillesse, ta disponibilité et ton soutien sans faille au cours de ce travail. Pour la qualité de ton enseignement de la gériatrie. Pour ton expertise clinique fine qui est, pour moi, un modèle dans l'exercice de la médecine.

A Monsieur le Professeur Denis MULLEMAN,
Pour m'avoir fait l'honneur de faire partie des membres de mon jury et pour l'intérêt que vous portez à ce travail.

A Madame le Docteur Nada IBRAHIM,
Pour l'honneur que tu m'as fait en acceptant de juger ce travail. Pour ton chaleureux accueil, ta bienveillance et ton enseignement passionné de la rhumatologie au cours de mon semestre à Orléans.

A Madame le Docteur Julie LORTHIOIS,
Pour l'honneur que tu m'as fait en acceptant de juger ce travail. Pour la confiance que tu m'as accordée au cours de mon stage au SSR d'Orléans et l'autonomie que tu m'as permise d'acquérir. Pour nos nombreuses discussions tant professionnelles que personnelles.

Au Professeur Mylène AUBERTIN-LEHEUDRE,
Pour m'avoir permis de travailler sur les données du laboratoire du muscle et de sa fonction (Montréal). Pour votre expertise pointue dans le domaine et vos conseils au cours de la réalisation de ce travail.

A toute l'équipe médicale de la Médecine Interne Gériatrique du CHU de Tours, au Docteur Marc MENNECART, au Docteur Joëlle BLEUET qui ont su me donner la passion de la Gériatrie dès l'externat et m'ont permis de découvrir les joies de cette merveilleuse spécialité.

A toute l'équipe médicale des Urgences d'Orléans pour leur accompagnement tout au long de mon semestre.

A toute l'équipe médicale du service de rhumatologie du CHR d'Orléans, au Docteur Nada IBRAHIM, au Docteur Carine SALLIOT, au Docteur Piera FUZIBET, au Docteur Kim NGUYEN, au Docteur Anis SOUSSI, au Docteur Rim BEN SAAD, au Docteur Saliha METRITER pour le goût de cette spécialité qu'ils m'ont fait partager et les connaissances qu'ils m'ont transmises.

A toute l'équipe médicale du Court Séjour Gériatrique du CHR d'Orléans, au Docteur Bénédicte COLSON, au Docteur Chau TRINH, au Docteur Marine PAMBET, au Docteur Véronique SKOWRONSKI, au Docteur Moez JALLOULI. Pour la qualité de la formation tant professionnelle qu'humaine reçue au cours de ce semestre et pour leur dévouement auprès des patients âgés. Pour la confiance qu'ils m'ont témoignée.

A toute l'équipe médicale du Soins de Suite et Réadaptation Gériatrique du CHR d'Orléans, au Docteur Sophie BALCON, au Docteur Julie LORTHIOIS, au Docteur Isabelle BATHELLIER, au Docteur Nathalie DOBIGNY. Pour leur bienveillance tout au long de ce semestre. Pour l'autonomie et l'assurance qu'elles m'ont permises d'acquérir.

A toute l'équipe médicale de l'Équipe Mobile Gériatrique du CHU de Tours, au Docteur Camille DEBACQ, au Docteur Léa LEMOINE, au Docteur Victoire LEROY, au Docteur Jacques-Alexis NKODO, au Docteur Agathe LEBAS, au Docteur Pierre-Alexandre HAZARD, au Docteur Amal AIDOUD. Pour m'avoir fait découvrir un autre exercice de la gériatrie.

A toutes les infirmières et infirmiers rencontrés depuis le début de mes années d'étude. Pour leur aide si précieuse au quotidien, pour leur amour de leur métier.

Aux aides-soignants, orthophonistes, diététiciennes, ergothérapeutes, secrétaires médicales, assistantes sociales, psychomotriciens, psychologues et tous ceux qui ont à cœur d'améliorer la prise en charge des patients gériatriques.

A mes co-internes,
A Claire, mon acolyte de promo, pour les bons moments passés ensemble tant en stage qu'autour d'une bière.
A Marine, pour nos projets « Loire à Vélo » revisités.
A Estelle et Gioia, pour nos petits resto Orléanais.
A Louise, pour nos virées piscine post-garde.
A Kaggwa, pour ton expertise sur les soins palliatifs, pour tout ce que tu m'as appris lors de notre stage en CSG à Orléans. Et pour toutes ces heures à refaire le monde en vocaux.
A mes co-internes de gériatrie pour toutes ces préparations de séances bibliographiques et pour ces moments partagés en congrès.
Mais également à Laury, Magalie, Nathan, Charlotte, Jean-Baptiste, Victoire, Simon, Lucie, Laura, Lila, Inès, Geoffrey rencontrés au fil de ces années.
Pour les joies, les galères et les fiertés partagées durant ce long cursus.

A Mme RUTARD, professeur de SVT au lycée, pour la qualité de votre enseignement, pour m'avoir encouragé à débuter ses longues années d'étude.

A mes amis, pour leur soutien sans faille durant ces années. Pour la joie à chaque retrouvaille.
A Raphi, pour cette longue et belle amitié depuis la maternelle. Pour tous ces merveilleux moments passés ensemble, toujours motivé pour partager de nouvelles expériences tant pour découvrir un petit resto breton que pour gérer une « bétonneuse ».
A Marie et Brieuc, pour nos aventures bretonnes principalement « guémenesques ». Pour cette complicité crée au fil des années.
A Laure, pour cette amitié depuis de nombreuses années, pour toutes les aventures vécues ensemble.
A Gisèle, pour nos soirées pizzas, pour ton gout de l'aventure contagieux. A Patrick, pour ton aide précieuse et ton implication sans faille à la préservation structurelle de notre maison.
A Romain et Lami, Marc et Manu, pour notre amitié et tous ces bons moments passés ensemble.

A ma famille, ma plus grande fierté.
A mes parents, pour avoir cru en moi depuis le début sans l'ombre d'un doute. Pour les belles valeurs que vous nous avez transmises. Pour votre présence réconfortante et votre amour.
A mon frère Cyprien et mes sœurs Marie et Claire, pour votre soutien et vos encouragements tout au long de ce parcours. Pour votre joie de vivre, pour cette complicité partagée et le bonheur de vous retrouver.
A ma marraine Sophie, pour tes conseils, ton soutien infaillible. Pour avoir été un pilier de ma vocation de médecin.
A mon oncle Jay et mes cousins Matthieu, David, Anne et Laure, pour ces merveilleux moments partagés en Auvergne, spéciale dédicace à la fête du Falgoux.
A mon parrain Philippe, pour nos discussions tant médiévales que mycologiques. A mes cousins, Louise et Marius.
A mes grands-parents maternels, pour la fierté de vos petits-enfants dans vos regards.
A mes grands-parents paternels, pour nos expéditions parisiennes parfois rocambolesques dont je garde un souvenir indélébile.
A ma belle-famille, pour m'avoir accueillie les bras ouverts.

A toi, Thibault, pour ta patience et ton soutien indéfectible tout au long de ses années. Tu auras su me ramener à la réalité bien plus d'une fois m'évitant de penser qu'uniquement la médecine occupait mes journées. Pour cet immense bonheur de vivre à tes côtés. A nos projets futurs, parce que l'avenir est devant nous.

A mes grands-parents,

SERMENT D'HIPPOCRATE

En présence des enseignants et enseignantes
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.

Je donnerai mes soins gratuits aux indigents,
et n'exigerai jamais un salaire au-dessus de mon travail.

Admis(e) dans l'intérieur des maisons, mes yeux
ne verront pas ce qui s'y passe, ma langue taira
les secrets qui me seront confiés et mon état ne servira pas
à corrompre les mœurs ni à favoriser le crime.

Respectueux(euse) et reconnaissant(e) envers mes Maîtres,
je rendrai à leurs enfants
l'instruction que j'ai reçue de leurs parents.

Que les hommes et les femmes m'accordent leur estime
si je suis fidèle à mes promesses.
Que je sois couvert(e) d'opprobre
et méprisé(e) de mes confrères et consœurs
si j'y manque.

Contents

INTRODUCTION:

Muscle and bone tissues form a unit, anatomical and functional, with constant evolving during life. With ageing the homeostasis between bone and muscle tends to deteriorate (1), that can lead to a pathological situation such as sarcopenia and osteoporosis (2).

Sarcopenia was firstly defined in 1988 as a "change in body composition and function" advancing with age, with a loss of muscle mass reaching a pathological threshold when it induces functional decline (3). The concept was completed with the notion of loss of muscle strength as it's currently defined (4). Although there is no international consensus on the definition, sarcopenia has been recognized as a pathological condition by the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code since 2016 (5). Muscle data could be assessed by a variety of methods including muscle biopsy, bioelectrical impedance analysis, computed tomography, magnetic resonance imaging, dual-energy X-ray absorptiometry or magnetic resonance spectroscopy. The impairment of muscle function leads to a decline in physical performances (6) and contributes to the loss of autonomy in daily and instrumental activites (7). Besides, the loss of muscle strength, known as dynapenia, has emerged as the primary predictor of functional decline when compared to the loss of muscle mass (8).
More recently, sarcopenia has been associated with low bone mineral density (4), with an increased risk of osteoporosis (9).

Osteoporosis is defined by a loss of bone mineral density (BMD) and abnormal bone microarchitecture heightening bone fragility and susceptibility to fractures (10). This insidious disease remains asymptomatic until a fracture occurs. Dual-energy X-ray absorptiometry (DXA) is the gold standard for the assessment of bone mineral density (11). However, previous studies have indicated that DXA measurements of bone mineral density may have limitations, as fractures can occur even in the presence of normal BMD (12). Analysis of trabecular and cortical bone microarchitecture can enhance the assessment of skeletal fragility and the prediction of fractures (13). High-resolution peripheral quantitative computed tomography (HR-pQCT) is a validated imaging technique to assess three-dimensional geometry and microarchitecture (14). Fractures are associated with altered geometrics parameters including cortical and trabecular volumetric bone mineral density, quantity and quality of the trabecular architecture, bone resistance of compressive and torsional strain (13,15). A recent meta-analysis which evaluated the most predictive bone HR-pQCT parameters of fragility fracture showed that cortical volumetric bone mineral density, trabecular thickness and stiffness (reflecting strength) are superior predictors (16).

As mentioned previously, the relationship between bone and muscle has been a subject of study in recent years, with a focus on pathological conditions of sarcopenia and osteoporosis. A newly emerging geriatric syndrome known as 'osteosarcopenia' was characterized by the co-occurrence of osteoporosis or osteopenia and sarcopenia. Few studies explored the prevalence of osteosarcopenia worldwide and the prevalence varies greatly between studies. In 2018, a meta-analysis found that osteosarcopenia occurs, including both gender, with a prevalence ranging from 5% to 37% (17). This association is a great concern as morbidity and mortality seems to be increased in this particular situation. Indeed, the prevalence of 1-year mortality was higher in patients with osteosarcopenia when compared to sarcopenia or osteoporosis alone (18). The coexistence of both conditions also increased the risk of falls and fragility fractures(19), leading to significant physical disability and loss of independence (20).

Many publications have explored the link between sarcopenia and impaired bone health. Individuals with confirmed sarcopenia had a poorer bone health (measured by DXA and pQCT) compared to those with

probable (low muscle strength only) or without sarcopenia (21). Lean mass, especially appendicular lean mass seems to be a strong parameter, predicting bone mineral density in DXA (22,23) . This finding underlines the importance of muscle mass analysis in predicting bone structure, but it is not always available in routine practice. Previous studies have demonstrated that clinical functional assessments such as Time Up and Go Test or grip test may also predict a deficient bone structure and the occurrence of fracture (24,25).
In older men, lower-limb relative appendicular lean mass and low physical performance (chair test and balance tests) are associated with bone microarchitecture decline (26).
Recently, it was showed that muscle strength (measured by grip strength and chair rising test) was associated with cortical rather than trabecular compartment parameters in HR-pQCT (27). Notably, authors did not include muscle mass data measured by DXA, being an integral part of the diagnostic criteria for sarcopenia. These associations were higher than those between muscle strength and BMD by DXA in previous studies (28). Furthermore, these studies were conducted in single genders, and data for both genders are lacking.

The aim of this study was to examine the influence of the muscular compartment on bone microarchitecture, assessed using HR-pQCT, by determining which muscle parameter is the most predictive of alteration in the bone compartment. We hypothesized that a higher muscle mass or strength was related to better bone architecture.

MATERIAL AND METHODS:

Design:

We performed a retrospective and cross-sectional study. All procedures were approved by the research ethics board at the Université du Québec à Montréal (Montréal, Québec, Canada) and all participants provided their written consent. The data was collected by trained clinical assessors from the university's Department of Physical Exercise Science in Montreal. This study was a secondary analysis of data collected from two previous studies (30, 31).

Setting and study population:

Voluntary participants were recruited from Montreal (Canada) community through various public communication channels.

Inclusion criteria were as follow: (1) age 60 years or over, (2) to have a low physical activity the previous 6 months (< 2 hours/week of planned exercises), (3) to have a stable weight (± 2 kg) over the previous 6 months, (4) no orthopedics disability, (5) no counter-indication to practice physical training (assessed using the Physical Activity Readiness Questionnaire (31)), (6) menopausal within the last 12 months, (7) non-smoker, (8) low alcohol consumption (≤ 2 drinks/day). Participants with untreated diagnoses of neurological, cardiovascular, lung or cognitive disease were excluded.

Data collection:

Anthropometrics data:

Body weight (kg) was determined using an electronic scale (Omron HB-500CAN, Oxford, UK) and height (m) using a stadiometer (Seca©, Hamburg, Germany). The Body Mass Index (BMI) was calculated according to the following formula: Body mass (Kg)/Height (m^2).

Body composition data:

Total body lean mass (total body LM (kg)), leg lean mass (LLM (kg)) and appendicular lean mass (AppLM (kg/m2)) were assessed by dual-energy X-ray absorptiometry (DXA) using Lunar Prodigy whole-body scanner (GE Medical Systems, Madison, WI, USA). The examination was performed in the supine position. Participants were asked to wear light clothing and remove heavy metal objects to avoid skewing the results. Indexes were used by dividing values of these variables by height^2 to have freed from the anthropometrics and sexes effects. Bone data such as total, spine and hip bone mineral density (g/cm2), hip and spine T-score were also quantified by DXA. Dual-energy X-ray absorptiometry (DXA) remains the gold standard for the assessment of bone mineral density by the calculation of T-score. Osteoporosis was defined by a T-score ≤ 2,5, osteopenia by a T-score between -1 and -2,5 (11). Sarcopenia was defined as appendicular lean mass/height^2 < 7 kg/m^2 for men and <15,5 kg/m^2 for women combined with dynapenia (grip test < 27 kg for men and < 16 kg for women)

Physical performance data:

Functional capacities were assessed using five clinical tests. The 4m walking test was performed at usual walking speed. The time (in seconds) required to cover the distance of 4m has been recorded. This objective test was measured to obtain the physical performance under comfortable conditions (32). The Time Up and Go Test (TUG, s)) was used at a comfortable and natural walking pace. Participants had to stand from a chair, walk a distance of 3 meters, turn around and sit down again. The pathological threshold retained was ≥ 20 seconds according to EWGSOP2 criteria (6). This test assessed physical mobility for frail older adults (33). To evaluate body-lower function, a chair stand test (in seconds) was conducted. It consisted of standing up and sitting down with arms folded across their chest as quickly as possible from a chair, ten times in a row.

The pathological cut-off for the Five Times Sit to Stand Test *{Citation}*is ≥ 15 seconds according to EWSOP2 criteria (6). Takai and al. have developed a power index from this test calculated by the following formula: Psit-stand (W) = [(L - 0,4) x body mass x g x 10] ÷ Tsit-stand; 0.4 (m) is the height of the standardized chair, L (m) is the leg length (from the great trochanter of the femur to the malleolus lateralis) and g (m/s2) represent the acceleration of gravity (9.8 m/s2) (34). The stair climbing test was measured to assess the lower limb strength, the balance and the ability to climb a flight of stairs in 20 seconds (35).

Mobility and aerobic capacity were assessed by the 6-minute walking test (in meters) (36). Participants were instructed to walk the longest distance as possible in 6 minutes. All walking test were registered using a treadmill (Gaitrite©, Biometrics, France).

The maximal isometric upper limb muscle strength was evaluated by the handgrip test (in newtons) with a handheld dynamometer (Lafayette© Instrument, Sagamore Pkwy N, IN, USA) (37). Handgrip strength was also expressed relative to body weight value (38), i.e. handgrip strength divided by the BMI (kg/m2) to have freed from the sex effects. For this test, participants hold the dynamometer in the hand with the arm at right angles and elbow to body. Concerning the lower limbs, knee extensor strength (newtons) was analyzed with a strain gauge system (Primus RS Chair, BTE) attached to chair on which participants were seated with hip joint angle at 90°(39).

Bone microarchitecture data:

The bone microarchitecture parameters were assessed using a peripheral quantitative computed tomography scan (Stratec XCT3000; STRATEC Medizintechnik GmbH). Bone data was collected from the scan of the right femur. The total length, voxel size (0.5 mm), and speed (10 mm/s) were included in the initial settings of pQCT software. Scans were performed by trained operators. Movement artefacts and their impact on image quality were visually analyzed by a second evaluator (40). Bone image analysis was performed with the open source software ImageJ (version 1.51q) and with the plugin BoneJ (Version 1.3.11).

Several types of bone data have been studied (15) : densities (cortical density and total density (mg/cm^3)), areas (cortical, trabecular and total areas (mm^2)). Two others measures reflecting bone strain (strength strain index, SSI (mm^3)) and compressive strength (BSI (g^2/cm^4)) were calculated by mathematic formula (41).

Data analysis

All analyses were performed with SPSS statistics (version 28.0.1.1., IBM Corp., Armonk, NY, USA). The results were considered statically significant at $p < 0,05$.

Descriptive statistics were used to analyze main characteristics of the population. Variable were described with the mean and the standard deviation. A normality test showed that all the variables follow a normal distribution according to the Kurtosis and skewness formula (42).

Pearson's correlations adjusted for age and sex were used to determine a correlation coefficient between physical performance and muscle variables with bone parameters. Correlation coefficients (r) were classified as follows: <0.3 weak; 0.3-0.6: moderate, >0.6: strong (43).

To evaluate the best muscle predictor to bone parameters, linear regressions using step by step model were performed using significant correlations. The coefficient of determination R and R^2were calculated.

RESULTS:

Baseline characteristics (see Table 1):
This study included 146 voluntary participants, mainly were men (men: n= 93, 64% and women: n=53, 36%). 54 participants (37%) were considered to have an osteopenia all sites combined according to the (36% in women and 38% in men. Osteoporosis only on spine was found in 7 men (4%). According to EGSOP2 sarcopenia cut-off points, 34 of men (23%) and 1 of women (2%) had a sarcopenia. The mean age was 67 years.
No difference was showed between women (respectively, mean ± SD 1,1 ± 0,1 g/cm², mean ± SD 1,2 ± 0,1 g/cm², p = 0,948) and men, according to total bone mineral density evaluated in DXA.
Concerning physical performance, men had better scores for the chair stand test (mean ± SD 19,7 ± 4,0 s for men and mean ± SD 20,8 ± 6,1 s for women, p < 0,01) and for the handgrip test according to the weight (mean ± SD 0,5 ± 0,1 s for men and mean ± SD 0,4 ± 0,1 s for women, p = 0,017). Any statistically significant difference was found for the others physical performance tests.
Body composition measured by DXA and bone microarchitecture parameters were similar between both sexes.

Relationship between physical performance and bone microarchitecture (see Table 2):
The cortical compartment analysis showed significant but weak correlations between cortical density and the stair climbing test, the maximal isometric upper and lower limb test and the 6-minute walking test (r = 0,174, p = 0,38; r = 0,242, p = 0,04; r = 0,219, p = 0,20; r = 0,238, p = 0,04; respectively). Moderate significant correlations were found between the cortical area and the power index of the chair stand test, developed by Takai and al., the 6-minute walking test, the maximal isometric lower limb muscle strength was found (r = 0,556, p < 0,001; r = 0,403, p < 0,001; r = 0,480, p < 0,001; respectively).
The total bone area analysis had similar correlations with cortical density, except for the power index of the chair stand which was also moderately correlated with the total bone area (r = 0,447, p < 0,001).
Concerning the trabecular compartment, only the power index of the chair stand was significantly correlated with trabecular area (r = 0,219, p = 0,015).
The strength strain and compressive indexes (SSI, BSI) were significantly correlated with the stair climbing test (SSI: r = 0,283, p < 0,001;BSI: r = 0,230, p = 0,006), the power index of the chair stand test (SSI: r = 0,492, p < 0,001; BSI: r = 0,410, p < 0,001), the 6-minute walking test (SSI: r = 0,339, p < 0,001;BSI: r = 0,378, p < 0,001) and the maximal isometric upper limb muscle strength (SSI :r = 0,432, p < 0,001; BSI: r = 0,452, p < 0,001).
Only negative but weak correlations were found between the 4m walking test and the following bone parameters: cortical area, SSI, BSI (r = -0,223, p = 0,011; r = -0,191, p = 0,022; r = -0,187, p = 0,025; respectively).
The power index of the chair stand, the 6-minute walking test and the maximal isometric lower limb muscle strength had strongest correlations with bone parameters, especially with the cortical area and the strength strain and compressive indexes.
The Time Up and Go Test was correlated with any variable.

Relationship between body composition and bone microarchitecture (see Table 3):
Moderate correlations were showed between lean mass indexes (total, lower limb and appendicular lean mass) and bone microarchitecture parameters, excepted for the cortical density.
Cortical, trabecular area and total bone area had positive significant correlations between total body lean mass (cortical area: r = 0,532, p < 0,001; trabecular area: r = 0,546, p < 0,001 ; total area: r = 0,527, p < 0,001), lower limb lean mass index (cortical area: r = 0,569, p < 0,001, trabecular area: r = 0,323, p < 0,001; total

area: r = 0,467, p < 0,001) and appendicular lean mass index (cortical area: r = 0,648, p < 0,001; trabecular area: r = 0,305, p = 0,001; total area: r = 0,499, p < 0,001). The strength strain and compressive indexes (SSI, BSI) were strongly correlated variables with the lean body mass (total lean mass index: r = 0,546, p < 0,001; r = 0,404, p < 0,001; lower limb lean mass index: r = 0,539, p < 0,001; r = 0,470, p < 0,001; appendicular lean mass index: r = 0,590, p < 0,001; r = 0,551, p < 0,001).
Total bone density correlated only with the appendicular lean mass index (r = 0,172, p = 0,042).

Regression between muscle compartment and bone microarchitecture (see Table 4):
Appendicular lean mass index was identified as the strongest positive influencing factor on cortical area (R = 0,600, p < 0,001) but also on strength and compressive indexes (SSI: R = 0,550, p < 0,001, BSI: R = 0,491, p < 0,001).
Total lean body mass index influenced positively and moderately total bone area (R = 0,535, p < 0,001).
Chair stand test was also shown to have a negative but weak effect with total bone density (R = - 0,245, p = 0,003). This negative correlation was due to the unit used: time in seconds.
Lastly, 6-minute walking test was positively weakly but significantly associated with cortical density (R = 0,085, p = 0,011).

DISCUSSION:

This cross-sectional study analyzed the relation between muscle data and bone microarchitecture. Our findings indicated that muscle mass and strength were significantly associated with bone microarchitecture, even after adjusting for both sex and age. Among the parameters assessed, the total body and appendicular lean mass were parameters which reflected the best the bone microarchitecture status.

The role of lean mass, especially appendicular, on the bone compartment is consistent with previous findings. Most previous studies establishing the relationship between bone and lean mass relied on absorptiometry measurements. These studies found that lean mass, and more specifically appendicular lean mass, was the main determinant of the total and site-specific BMD (39 – 41). In the MINOS cohort, a decrease in appendicular lean mass was linked to altered bone size, particularly cortical thickness (47). A low lean mass reduced the bending strain in DXA analysis (47,48). However, in literature, microarchitecture analysis and fracture risk prediction limitations of the DXA were widely demonstrated. To address these limitations, we opted to use microscanner-derived bone data, allowing for a more detailed assessment of bone architecture
Bone deformation capacity under stress, crucial in the occurrence of fractures, was specifically analyzed. To our knowledge, only a few studies have investigated the role of bone strain index in DXA and in HR-pQCT as a predictor of the risk of occurrence of fracture (21,49). In our study, appendicular lean mass was found to be the best correlate with strain indexes (BSI and SSI), indicative of the bone structural stiffness and strength.

Moreover, the relationship between lean mass and bone microarchitecture found in our study was also congruent with the literature. Bone area data (cortical, trabecular and total) were significantly associated with lean mass in the present study. This association was stronger between lean mass and cortical area. In the same line, in cohorts of aged more 60 years populations, lean mass was positively associated with the cortical compartment (15,48). Two others studies from an older men prospective cohort highlighted that a low appendicular upper-limb lean mass was associated not only to a decrease in bone mineral content but also to altered trabecular density, despite an increase of aera, and the cortical compartment (50, 51). Indeed, it was demonstrated that trabecular compartment was mainly and firstly altered during osteoporosis, induced a decrease or even disappearance of the number and thickness of bone trabeculae. This would increase the load resting on the cortical bone which could lead to cortical porosity and trabecularization of the inner cortical layer (52,53).

Furthermore, we found a relationship between muscle strength, physical performance and bone microarchitecture. Positive correlation between grip test and bone architecture, especially cortical density and strain index was found. The literature on this subject is extensive and majority of authors agree on the association between a dynapenia and bone density (54–56), predicting the risk of osteoporosis (57). Moreover, 6-minute walking test was positively associated with cortical density. To our knowledge, no prior study has investigated the relationship between this endurance parameter and bone architecture. No statistical link was demonstrated between the timed up and go test and the bone compartment, as found in other study, even if it is controversial. Therefore, previous studies have found a link between TUG and osteoporosis fracture risk independently of BMD (25,58). This suggests that while TUG predicts falls, it may not directly impact the bone compartment.
We also showed a negative association between the chair stand test performances and the total femoral bone density. Literature is still controversial as a recent study did not found an association between physical performance tests (chair stand test, handgrip test, gait speed, lower limb muscle strength) and hip BMD or fracture risk (59). The difference in results between our work and this study could be due to the bone method assessment.

Some physiopathological hypothesis could explain our results. Firstly, the "mechanostat" theory illustrated the effect of mechanical loads, applied by muscle, cause deformations or strains on bone, guaranteeing a balance on bone formation and resorption (60). This phenomenon was mediated by mechanoreceptors on osteocytes (61), more sensitive in endocortical than in periosteal tissue (62). So bone could adapt increasing its cortical area (27), as it was suggested in our results. The association between muscle mass and strength and their effect on bone size and structure was previously described in young people (63) and strongly persisted throughout life, including in nonagenarians (64).
It was also demonstrated that the muscle size was more strongly linked than the muscle strength on bone compartment (65) by increasing absolute forces applied to the bone.
The results of our study suggested that, the loading effect imposed by the muscle on the bone seemed to be regional. We have shown a positive correlation between lower limbs muscle strength and femoral bone microarchitecture. Similar results were found in the literature. Former studies highlighted an association between lower limb muscle strength and hip mineral density (59,66), whereas no relationship was described with the BMD spine (67) referring to a muscle-bone unit effect. But this hypothesis is unclear in the literature. Indeed, some authors found a significant association between lean mass and femoral neck BMD independently from muscle loading (68). Others found no association between leg lean mass and the occurrence of hip fracture while total lean mass increases the risk (69). The decreasing physical activity level with ageing incompletely explained the bone loss (64). They highlighted the potential involvement of systemic factors influencing both muscle and bone phenotypes and their interaction. Several molecular factors, especially from IGF signaling pathway (70) and specific cytokines get involve in bone-muscle homeostasis (71).

This study had some limitations. First of all, this was a transversal study, and no causal relationship can be established. Secondly, recruitment of patients was on voluntary basis, leading to a selection bias. The patient selection criteria were based on the absence of comorbidities and a poor level of physical activity. We probably selected a population with a better health status, even if sedentary, than the general population.
Moreover, about body composition, lean mass data were analyzed in DXA could be falsely increased by fat mass and total body water (72). Therefore, literature was controversial concerning the effect of lean mass on bone compartment. Some studies have found that appendicular fat mass best predicted altered bone mineral density compared to others body composition parameters (73,74). Furthermore, we didn't analyze the effect of common determinants reflecting bone and muscle condition such as nutritional status.

Our results suggested that a lower lean mass and muscle strength weaken bone structure. It was widely demonstrated that a low lean mass leading to clinical events such as falls (74) and fragility fractures (75). A long prospective study revealed an altered bone microarchitecture, especially trabecular parameters played a role in the occurrence of all types of incident fractures (76). A recent meta-analysis confirmed these results, by demonstrating that cortical density, trabecular thickness and bone constraint from HRpQCT data were the most predictive parameters of osteoporotic fractures (16).
To prevent falls, fractures and their consequences on independence, it's widely agreed that physical activity play a pivotal role. Resistance training and high-impact weight-bearing physical activities had a greater impact on BMD than walking exercise (77). It was demonstrated that resistance training exercises have a common action of preventing bone and muscle loss in particular accompanied by a charging port (78).Thus, it seems that specific physical activity programs, similar to those recommended for the management of sarcopenia could be recommended to also protect the bone compartment.

To conclude, total and appendicular lean mass appeared best predictors of a bone microarchitecture in HR-pQCT analysis, especially for bone area and bone strain stress in a young older population. These results

provide the evidence that lean mass evaluation in clinical practice, could help physicians screen older patients with bone fragility. Further longitudinal studies are necessary to strengthen the relationship between the lean mass and the bone microarchitecture and their role in fragility fracture risk.

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TABLES

Table 1 – Baseline Characteristics of the Patients.

Characteristics	All participants (n =146)	Male (n=93)	Female (n=53)	p-value
Demographic factors				
Age (years)	67,3	67,2	67,6	0,651
Taille (cm)	168 ± 0,1	168 ± 0,1	167 ± 0,1	0,581
BMI (kg/m2)	28,6 ± 5,2	27,5 ± 4,1	30,5 ± 6,3	0,02
Sarcopenia according to EWGSOP2 (%)	24% (n = 35)	37% (n = 34)	2% (n = 1)	
Physical performance				
Functional capacities				
4m walking test (s)	3,0 ± 0,4	2,9 ± 0,4	3,1 ± 0,5	0,038
Time up and go (s)	10,0 ± 1,6	9,9 ± 1,6	10,2 ± 1,7	0,235
Chair stand test (s)	20,1 ± 4,9	19,7 ± 4,0	20,8 ± 6,1	0,223
Stair climbing test (nb/20s)	29,6 ± 5,7	31,3 ± 5,0	26,7 ± 5,8	< 0,01
Power index of chair stand test (W)	165,2 ± 51,7	162,9 ± 49,7	169,3 ± 55,2	0,474
Mobility and aerobic capacity				
6-minute walking test (m)	571,6 ± 91,3	578,6 ± 90,5	559,4 ± 92,3	0,221
Muscle strength, quality and power				
Handgrip strength/body weight (N/kg)	0,4 ± 0,1	0,5 ± 0,1	0,4 ± 0,1	0,017
LLMS (N)	337,0 ± 108,4*	346,5 ± 111,5$	311,5 ± 96,7¶	0,125
Body composition by DXA				
Appendicular LM index (kg/m²)	8,1 ± 1,2	8,1 ± 1,2	8,2 ± 1,1¶	0,779
Lower limb LM index (kg/m²)	6,2 ± 0,8	6,2 ± 0,8	6,3 ± 0,8	0,551
Total LM index (kg/m²)	17,4 ± 2,3	17,2 ± 2,1	17,7 ± 2,6	0,245
T-score hip	-0,3 ± 1,0*	-0,3 ± 1,1$	-0,4 ± 0,9¶	0,264
T-score spine	-0,0 ± 1,6*	0,0 ± 1,2$	-0,3 ± 1,4¶	0,185
Total BMD (g/cm²)	1,2 ± 0,1	1,2 ± 0,1	1,2 ± 0,1	0,948
BMD spine (g/cm²)	1,2 ± 0,2*	1,2 ± 0,2	1,2 ± 0,2¶	0,369
BMD hip (g/cm²)	1,0 ± 0,1*	1,0 ± 0,2	1,0 ± 0,1¶	0,611
Bone microarchitecture by pQCT				
Cortical density (mg/cm³)	1095,5 ± 31,8	1096,7 ± 29,4	1093,5 ± 35,9	0,562
Cortical area (mm²)	399,3 ± 62,3*	398, 7 ± 56,9$	400,4 ± 71,6¶	0,890
Total density (mg/cm³)	712,5 ± 92,1	709,7 ± 76,6	717,5 ± 115,1	0,660
Total area (mm²)	646,3 ± 105,8*	646,6 ± 104,0$	645,9 ± 110,2¶	0,974
Trabecular area (mm²)	116,0 ± 45,5*	117,8 ± 44,8$	112,5 ± 47,1¶	0,546
SSI (mm³)	3053,4 ± 700,3	3092,3 ± 681,9	2985,1 ± 732,9	0,375
BSI (g²/cm⁴)	3,3 ± 0,8	3,2 ± 0,7	3,3 ± 0,9	0,832

Abbreviations: BMI = body mass index; LLMS = lower limb muscle strength; BMD = bone mineral density; LM = lean mass; SSI = strength strain index; BSI = bone strain index.
Data are presented with the mean ± SD.
*Number participants: * (n = [114;146[), $ (n = [83;93]), ¶ (n = [28;53])*

Table 2 – Correlations between physical performance tests and bone microarchitecture parameters

	CoD (mg/cm^3)	**CoA** (mm^2)	**ToD** (mg/cm^3)	**ToA** (mm^2)	**TrA** (mm^2)	**SSI** (mm^3)	**BSI** (g^2/cm^4)
Functional capacities							
4m walking test (s)	- 0,108	- 0,223*	- 0,081	- 0,127	- 0,032	- 0,191*	- 0,187*
Time up and go (s)	- 0,094	- 0,104	- 0,136	- 0,005	0,123	- 0,056	- 0,151
Chair stand test (s)	- 0,052	- 0,129	- 0,224*	0,111	0,148	0,029	- 0,193*
Stair climb test (nb/20s)	0,174*	0,271*	0,053	0,228*	0,078	0,283*	0,230*
Power index of chair stand test (W)	0,017	0,556*	0,073	0,447*	0,219*	0,492*	0,410*
Mobility and aerobic capacity							
6-minute walking test (m)	0,238*	0,403*	0,184*	0,224*	0,075	0,339*	0,378*
Muscle strength, quality and power							
Handgrip strength/ body weight (N/kg)	0,242*	0,159	- 0,037	0,195*	0,062	0,273*	0,105
LLMS (N)	0,219*	0,480*	0,176	0,295*	0,024	0,432*	0,452*

Correlations were conducted using Pearson's correlation test adjusted for sex and age, and results presented correspond to the correlation coefficient (r). Abbreviations: CoD = Cortical density, CoA = Cortical area, ToD = Total density, ToA = Total area, TrA = Trabecular area, SSI = Strength strain index, BSI = bone strain index, LLMS = lower limb muscle strength

*: p-value < 0,05

Table 3 – Correlations between lean mass by DXA and bone microarchitecture parameters

	CoD (mg/cm3)	**CoA** (mm^2)	**ToD** (mg/cm^3)	**ToA** (mm^2)	**TrA** (mm^2)	**SSI** (mm^3)	**BSI** (g^2/cm^4)
Appendicular LM index (kg/m^2)	0,100	0,648*	0,172*	0,499*	0,305*	0,590*	0,551*
Leg LM index (kg/m^2)	0,044	0,569*	0,120	0,467*	0,323*	0,539*	0,470*
Total LM index (kg/m^2)	- 0,033	0,532*	0,036	0,527*	0,368*	0,546*	0,404*

Correlations were conducted using Pearson's correlation test adjusted for sex and age, and results presented correspond to the correlation coefficient (r).
Abbreviations: CoD = Cortical density, CoA = Cortical area, ToD = Total density, ToA = Total area, TrA = Trabecular area, SSI = strength strain index, BSI = bone strain index, LM = lean mass
*: p-value < 0,05

Table 4 – Results of a linear regression step by step model analyzing muscle parameters most associated with bone microarchitecture parameters assessed by HR-pQCT

Bone microarchitecture variables	**Muscle data most associated with bone microarchitecture**	**Standardized regression coefficients**	**R^2 adjusted**	**p-value**
Cortical density (mg/cm^3)	6-minute walking test	0,085	0,058	**0,011**
Cortical area (mm^2)	Appendicular lean mass index	0,600	0,354	**< 0,001**
Total density (mg/cm^3)	Chair stand test	- 0,245	0,054	**0,003**
Total area (mm^2)	Total lean body mass index	0,535	0,279	**< 0,001**
Trabecular area (mm^2)	Total lean body mass index	0,362	0,124	**< 0,001**
SSI (mm^3)	Appendicular lean mass index	0,550	0,296	**< 0,001**
BSI (g^2/cm^4)	Appendicular lean mass index	0,491	0,235	**< 0,001**

Abbreviations: SSI = strength strain index, BSI = compressive strength index

Ginestet Cécile
33 pages – 4 tableaux

Résumé :
Introduction : L'ostéoporose et la sarcopénie sont des conditions liées à l'âge, partageant des caractéristiques communes, et augmentant respectivement le risque fracturaire et le déclin des capacités physiques. L'étude osseuse tridimensionnelle permet l'analyse quantitative et qualitative de la microarchitecture osseuse et prédit avec plus de précision le risque de fracture de fragilité que la technique de référence (absorptiométrie biphotonique à rayons X, DEXA).
Objectif : L'objectif de l'étude était d'étudier la relation entre des données musculaires et la microarchitecture osseuse évaluée par un microscanner osseux et de déterminer quelle variable musculaire était la plus prédictive des paramètres de microarchitecture osseuse.
Méthodologie : Nous avons réalisé une étude transversale, incluant des participants, âgés de 60 à 81 ans, sédentaires, vivant dans la communauté de Montréal au Québec. Les paramètres musculaires et osseux ont été recueillis par DEXA et microscanner osseux de haute résolution (densité et aire corticale, densité et aire trabéculaire, index biomécanique). Plusieurs tests fonctionnels utilisés en pratique clinique ont également été collectés pour étudier les performances physiques. Il a été réalisé des corrélations ajustées sur le sexe et l'âge et une régression linéaire à partir des corrélations statistiquement significatives.
Résultats : 146 participants ont été inclus. Parmi les participants, 37% (n= 54) présentaient une ostéopénie et 4% (uniquement des hommes) présentaient une ostéoporose vertébrale selon le T-score en DEXA. 23% des participants (n = 35) étaient considérés comme sarcopéniques.
Des corrélations positives étaient retrouvées entre la masse maigre totale et appendiculaire et les paramètres osseux évalués en HR-pQCT. Il a été mis en évidence que la masse maigre appendiculaire était le facteur le plus prédictif concernant l'aire corticale ($R = 0{,}600$, $p < 0{,}001$), mais également des index de contrainte osseuse (SSI : $R = 0{,}550$, $p < 0{,}001$, BSI : $R = 0{,}491$, $p < 0{,}001$). La masse maigre totale était le paramètre le plus prédictif concernant l'aire osseuse totale ($R = 0{,}535$, $p < 0{,}001$) et l'aire trabéculaire ($R = 0{,}362$, $p < 0{,}001$).
Conclusion : Dans une population québécoise d'âge moyen, la plupart des paramètres musculaires et fonctionnels semblent liés à la microarchitecture osseuse. Cependant, la masse maigre est le facteur le plus prédictif et donc un indicateur pertinent à utiliser dans l'étude de la relation muscle-os.

Mots clés :
Microarchitecture osseuse, masse maigre, ostéoporose, sarcopénie, tomodensitométrie osseuse

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Date de soutenance : 16 octobre 2023