General

Osteosarcopenia and type 2 diabetes mellitus in post-menopausal women: a case-control study

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Background

Osteosarcopenia has been defined as the concomitance of low bone density (osteopenia/osteoporosis) and sarcopenia. Osteoporosis is characterized by alterations in bone microarchitecture and decrease of bone mineral density (BMD), whereas sarcopenia is the progressive decrease of both muscle mass and function that increase the risk of falls. Type 2 diabetes mellitus (T2DM) is associated with poor bone strength and muscle wasting.

Objective

The aim of this study is to analyze the association between osteosarcopenia and T2DM in post-menopausal women (PMW).

Methods

We performed an age matched case-control study (1:2 ratio), considering as cases PMW affected by T2DM, and PMW without T2DM as control group. For all patients a DXA evaluation to investigate bone density and body composition measures were performed. Moreover, we carried out muscle strength and performance assessments. Outcome measures were femoral neck and lumbar spine BMD T-scores, appendicular lean mass (ALM), handgrip strength and the Short Physical Performance Battery (SPPB). Data from both groups were analyzed and compared.

Results

Thirty-six PMW (12 T2DM vs 24 non-T2DM) were recruited. The frequency of osteosarcopenia was significantly higher in the T2DM group compared to controls (50% vs 17%; OR 5.0, 95% CI 1.05 to 23.79, p = 0.043). Handgrip strength was significantly lower in the T2DM group (10.09 ± 4.02 kg vs 18.40 ± 6.83 kg; p = 0.001).

Conclusions

Post-menopausal women with T2DM have a 5 times higher risk to have osteosarcopenia compared to non-diabetic ones. Further studies on larger cohorts are required to confirm these findings.

INTRODUCTION

Body composition is critical to determinate health or disease.[1] Skeletal muscle and bone interact through autocrine, paracrine, and endocrine modulators to maintain muscle and bone homeostasis.[2–5] From a clinical perspective osteopenia/osteoporosis and sarcopenia are chronic musculoskeletal conditions with increasing incidence with aging.[6] Osteoporosis is characterized by alterations in bone microarchitecture and decrease of bone mineral density (BMD), whereas sarcopenia is defined by a progressive decrease of muscle mass and function that reduce independence in activities of daily living (ADLs) and quality of life.[6,7]

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The concomitance of sarcopenia and osteoporosis has been defined as a "dangerous duet" to describe the association between the progressive deterioration of muscle mass and function that affects older people and bone fragility causing a large percentage of late-life disability.[8]

This concomitance was named osteosarcopenia to identify a new nosological entity, operationally defined as the concomitance of osteopenia/osteoporosis and sarcopenia in the same patient.[9]

The main clinical implication of this association is the increased risk of fragility fractures, considering that sarcopenia increases the risk of fall and osteoporosis reduces bone strength.[9–13]

Some risk factors, such as level of physical activity and metabolic disorders, are shared by osteoporosis and sarcopenia according to literature. Several endocrine diseases, including type 2 diabetes mellitus (T2DM), affect both bone and muscle health resulting in impaired bone quality and muscle wasting.[14–16]

Despite the high prevalence of T2DM and its relationship with bone and muscle health, the link between this condition and osteosarcopenia has not yet been well investigated. So, the aim of the present study is to estimate the risk of osteosarcopenia in post-menopausal women (PMW) with T2DM.

MATERIALS AND METHODS

STUDY DESIGN

An observational case-control study was conducted by enrolling PMW with or without T2DM attending the outpatient service for the management of metabolic bone disorders and skeletal muscle diseases of the University of Campania "Luigi Vanvitelli", Naples, Italy, from March 2021 to June 2021.

ETHICAL CONSIDERATIONS

Patients were enrolled after reading, understanding, and signing a written informed consent form, approved by the Ethical Committee of our institution.

PARTICIPANTS

The cases were represented by women diagnosed with T2DM treated with insulin, while controls were age-matched non-diabetic women with a 1:2 proportion. Exclusion criteria were obesity (BMI>30), cancer, severe depression, cognitive impairment affecting protocol adherence, poor compliance to clinical evaluation, severe disease-related complications (e.g., diabetic foot, coronary heart disease, retinopathy). Participants took part in the study protocol in a single time.

OUTCOME MEASURES

Personal and anamnestic data (age, date of birth, comorbidities) were collected. Body weight (Kg) was measured using mechanical balance scales (with 0.1 kg approximation) while height (cm) was measured using a stadiometer as we considered the mean value of two subsequent measurements (0.1 cm approximation). The Body Mass Index (BMI) was calculated using the accepted formula (BMI= weight/height,^{2} kg/m^2) and overweight and obesity were assessed according to WHO guidelines.[17] Physical Activity was evaluated using International Physical Activity Questionnaire (IPAQ).[18]

Handgrip strength was measured using a JAMAR hydraulic dynamometry. We considered the best of three measurements (kg) on the dominant hand (0.1 kg approximation). The Short Physical Performance Battery (SPPB) was also administered for muscle performance assessment. Patients were subjected to DXA (Dual-energy X-ray Absorptiometry) (iDXA GE-Lunar) for the measurement of muscle mass and BMD. For each patient we made one total body scan, one left femoral scan and one lumbar spine scan. In particular, Appendicular Lean Mass (ALM, kg), femoral neck and lumbar spine BMD (g/cm2) and T-scores were considered.

Osteosarcopenia was defined as low BMD (<-1 SD) and/or prevalent fragility fractures + poor muscle mass (ALM <15 kg) and muscle weakness (HGS<16 kg) and/or poor muscle performance (SPPB<8).

STATISTICAL ANALYSIS

Statistical analysis was carried out using Statistical Package for the Social Sciences 25 (SPSS 25) software to perform Student's t-test, after applying Levene's test for variance. Moreover, odds ratios were calculated for non-continuous variables.

RESULTS

We enrolled 36 women (12 T2DM and 24 controls). Patients' demographic and anthropometric characteristics are shown in Table 1. No differences were found between the two groups in terms of age, weight, height, and BMI.

In Table 2 the outcome measures in cases and controls are reported. Cases showed significantly lower handgrip strength (10.09 ± 4.02 kg vs 18.40 ± 6.83 kg, p = 0.001) and higher prevalence of osteosarcopenia (50% vs 17%; OR 5.0, 95% CI 1.05 to 23.79, p = 0.043) compared to controls, while no between-group significant differences were reported for the risk of falls (OR 1.0, 95% CI 0.20-4.95) and fragility fractures (OR 3.57, 95%CI 0.64-19.97, p=0.134). All other outcomes were not significantly different between the two groups.

DISCUSSION

The relationship between T2DM and osteosarcopenia has not yet been widely investigated, although it is well known that diabetes mellitus leads to musculoskeletal wasting. The aim of this study was to estimate the risk of osteosarcopenia in PMW with T2DM.

Fahimfar et al (2020) found that diabetes has a direct association with osteosarcopenia in men.[19] Our study confirms this association also in PMW and, as no between-

Table 1. Study population characteristics

Parameters	T2DM women (n=12)	Non-T2DM women (n=24)	p-value
Age (y)	65.33 ± 9.47	64.79 ± 5.89	0.858
Weight (kg)	57.83 ± 10.30	58.13 ± 8.26	0.927
Height (m)	1.54 ± 0.05	1.57 ± 0.06	0.095
BMI (kg/m²)	24.32 ± 3.54	23.45 ± 2.76	0.426

Table 2. Outcome measures for the assesment of physical activity, muscle mass and function, bone mineral density, falls and fractures.

Outcomes	T2DM women (n=12)	Non-T2DM women (n=24)	p-value
Physical Activity level			
- **none**	8 (67 %)	13 (54%)	0.475
- **low**	3 (25%)	2 (8.5%)	0.192
- **medium**	1 (8%)	7 (29%)	0.184
- **high**	0 (0%)	2 (8.5%)	0.520
Handgrip strength (kg)	10.09 ± 4.02	18.40 ± 6.83	0.001
ALM (kg)	14.34 ± 2.20	14.26 ± 2.43	0.916
Femoral neck T-score	-2.38 ± 0.70	-2.35 ± 0.78	0.889
Lumbar spine T-score	-1.89 ± 1.01	-2.63 ± 1.08	0.058
SPPB < 8	7 (58%)	9 (38%)	0.240
Osteosarcopenia	6 (50%)	4 (17%)	0.043
Falls	3 (25%)	6 (25%)	1
Fragility fractures	10 (83%)	14 (58%)	0.134

group differences in BMI and levels of physical activity were found, T2DM seems to be a risk factor for osteosarcopenia independently from BMI and physical activity.

Our results may be linked to the characteristics of the chosen population. Indeed, our study focused only on female while, in contrast with our findings, *Fahimfar et al (2020)* reported that having osteosarcopenia was more likely in diabetic men (PR 1.33, 95% CI 1.04–1.69), but not in women.[19] Moreover, we decided to exclude obese women, as not to be influenced by an additional metabolic disorder but to focus only on T2DM effects. Indeed, our population showed mean BMI values within normal range and no significant between-group difference in terms of BMI. In a recent study, an inverse association between BMI and osteosarcopenia was found,[20] although further investigations are needed to clarify which is the role of fat mass on muscle and bone in T2DM patients, even using body composition techniques. Moreover, in our population, no significant between-group difference was found in terms of levels of physical activity, even if diabetic patients were more likely doing none or low physical activity. A recent study reported significant association between physical activity and osteosarcopenia in men, but not in women.[19] Therefore, future studies are needed to identify the role for mechanical versus biochemical stimuli on muscle-bone crosstalk in T2DM, taking into account also the gender, even using direct and continuous measures for performed physical activity.

In our study, no significant between-group differences for falls and fragility fractures were found. This may be due to the high number of fractures in the control group (58%) probably related to the setting (center for the management of osteoporosis), in which the number of patients with bone fragility is likely to be high. Even if an increased fragility fracture risk was not demonstrated in our population, from a pathophysiological point of view we can hypothesize that fracture risk in patients with T2DM is increased, despite BMD, because of other mechanisms, such as poor bone quality, sarcopenia, and increased fall risk.[21,22]

LIMITATIONS

The main study limitations are the small sample size and no data about other disease-specific medications for T2DM, considering that all cases were treated with insulin. Future perspectives should include the investigation of sub-groups based on serum glucose levels and insulin-resistance and to investigate the role of different T2DM drugs on bone turnover, muscle metabolism and on the risk of falls and fractures in patients with osteosarcopenia.

CONCLUSIONS

Post-menopausal women with T2DM have a significant higher risk to have osteosarcopenia compared to non-diabetic ones. Our study suggests that osteosarcopenia should

be early identified and treated in diabetic patients to prevent its consequences, although its role in terms of risk of falls and fractures in this population should be better defined in prospective studies.

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AUTHOR CONTRIBUTIONS

The authors contributed equally.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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None.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

REFERENCES

1. Gillette-Guyonnet S, Vellas B. Body composition and age-related diseases. *Mech Ageing Dev*. 2003;124(3):247-248.

2. Hoffmann C, Weigert C. Skeletal Muscle as an Endocrine Organ: The Role of Myokines in Exercise Adaptations. *Cold Spring Harb Perspect Med*. 2017;7(11):a029793.

3. Morley JE. Frailty and sarcopenia in elderly. *Wien Klin Wochenschr*. 2016;128(Suppl 7):439-445. doi:10.1007/s00508-016-1087-5

4. Stefanaki C, Pervanidou P, Boschiero D, Chrousos GP. Chronic stress and body composition disorders: implications for health and disease. *Hormones (Athens)*. 2018;17(1):33-43.

5. Girgis CM, Baldock PA, Downes M. Vitamin D, muscle and bone: Integrating effects in development, aging and injury. *Mol Cell Endocrinol*. 2015;410:3-10.

6. Greco EA, Pietschmann P, Migliaccio S. Osteoporosis and Sarcopenia Increase Frailty Syndrome in the Elderly. *Front Endocrinol (Lausanne)*. 2019;10:255.

7. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010;39(4):412-423.

8. Crepaldi G, Maggi S. Sarcopenia and osteoporosis: A hazardous duet. *J Endocrinol Invest*. 2005;28(10 Suppl):66-68.

9. Paintin J, Cooper C, Dennison E. Osteosarcopenia. *Br J Hosp Med (Lond)*. 2018;79(5):253-258.

10. Huo YR, Suriyaarachchi P, Gomez F, et al. Phenotype of osteosarcopenia in older individuals with a history of falling. *J Am Med Dir Assoc*. 2015;16(4):290-295.

11. Yoo JI, Kim H, Ha YC, Kwon HB, Koo KH. Osteosarcopenia in Patients with Hip Fracture Is Related with High Mortality. *J Korean Med Sci*. 2018;33(4):e27.

12. Iolascon G, Moretti A, Giamattei MT, Migliaccio S, Gimigliano F. Prevalent fragility fractures as risk factor for skeletal muscle function deficit and dysmobility syndrome in post-menopausal women. *Aging Clin Exp Res*. 2015;27(Suppl 1):S11-16.

13. Borgström F, Karlsson L, Ortsäter G, et al. Fragility fractures in Europe: burden, management and opportunities. *Arch Osteoporos*. 2020;15(1):59.

14. Yoo JI, Ha YC. Review of Epidemiology, Diagnosis, and Treatment of Osteosarcopenia in Korea. *J Bone Metab*. 2018;25(1):1-7. doi:10.11005/jbm.2018.25.1.1

15. Hirschfeld HP, Kinsella R, Duque G. Osteosarcopenia: where bone, muscle, and fat collide. *Osteoporos Int*. 2017;28(10):2781-2790. doi:10.1007/s00198-017-4151-8

16. Kawao N, Kaji H. Interactions between muscle tissues and bone metabolism. *J Cell Biochem*. 2015;116(5):687-695. doi:10.1002/jcb.25040

17. World Health Organization. Obesity and overweight. Published 2018. Accessed October 28, 2021. https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight

18. Hallal PC, Victora CG. Reliability and validity of the International Physical Activity Questionnaire (IPAQ). *Med Sci Sports Exerc*. 2004;36(3):556. doi:10.1249/01.mss.0000117161.66394.07

19. Fahimfar N, Zahedi Tajrishi F, Gharibzadeh S, et al. Prevalence of Osteosarcopenia and Its Association with Cardiovascular Risk Factors in Iranian Older People: Bushehr Elderly Health (BEH) Program. *Calcif Tissue Int*. 2020;106(4):364-370.

20. Okamura H, Ishikawa K, Kudo Y, et al. Risk factors predicting osteosarcopenia in postmenopausal women with osteoporosis: A retrospective study. *PLoS One*. 2020;15(8):e0237454.

21. Li G, Prior JC, Leslie WD, et al. Frailty and Risk of Fractures in Patients With Type 2 Diabetes. *Diabetes Care*. 2019;42(4):507-513.

22. Sarodnik C, Bours SPG, Schaper NC, van den Bergh JP, van Geel TACM. The risks of sarcopenia, falls and fractures in patients with type 2 diabetes mellitus. *Maturitas*. 2018;109:70-77. doi:10.1016/j.maturitas.2017.12.011