Association between muscle power and bone mineral density in patients with anorexia nervosa

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ABSTRACT

Purpose: The relationship between bone mineral density (BMD) and muscle performance is little investigated in the context of eating disorders. The aim of the present study was to evaluate the association between BMD and lower-limb muscle power in patients with anorexia nervosa (AN).

Methods: 44 female patients (aged 12 to 40 years) with AN were included in the study. The 5-repetition sit-to-stand test was conducted to assess physical functionality, and both absolute and relative muscle power were calculated. Body composition, appendicular lean mass (ALM), and BMD were measured using dual-energy X-ray absorptiometry.

Results: A significant association was observed between lower-limb absolute muscle power and lumbar BMD. This association was still significant after adjustment for ALM.

Conclusions: Our results show a positive relationship between lumbar BMD and lower-limb muscle power in patients with AN, which cannot be solely accounted for by ALM.

KEYWORDS

Bone mineral density, anorexia nervosa, functional test, eating disorder.

Introduction

Anorexia nervosa (AN) is a psychiatric disease with significant somatic impairment secondary to low body mass, restrictive eating, and dietary inadequacy [1]. In patients with AN, malnutrition-induced derangements in multiple hormonal axes have been described, causing reduced circulating oestrogen and IGF-1 levels, hypercortisolaemia and growth hormone resistance; the above-mentioned hormonal alterations, combined with energy deprivation and nutrient deficiencies, can detrimentally affect bone mineral density (BMD) [2]. Indeed, insufficient calcium and vitamin D dietary intake may further contribute to reduced BMD.

Low BMD is an early complication of AN, significantly increasing fracture risk in these patients [3,4]. Bone microarchitecture is usually altered in both the cortical and trabecular compartments, as shown by higher cortical porosity and trabecular separation due to reduced cortical bone area and trabecular number, respectively [5,6].

In the presence of undernutrition, bone fragility and fracture risk are further increased in subjects who have not yet achieved skeletal maturity, with undernutrition leading to insufficient growth and a blunted bone density growth peak. Those alterations are associated with a lower fracture threshold, even when undernutrition has been resolved [7].

BMD is related to appendicular muscle mass, which is reduced in individuals with AN. Since the timing of peak bone mass roughly coincides with that of peak muscle mass, optimizing muscle mass growth trajectories during the first decades of life can positively affect skeletal growth and help to mitigate the potential onset of osteosarcopenia later in life. This is especially important given that BMD is both a marker of general health and an independent predictor of mortality [8].

A number of studies showed a predictive role of both muscle mass and body fat on BMD [9,10], especially in specific populations, such as the elderly, who experience a parallel decline in muscle strength and BMD [11], or in pre- and postmenopausal women, in whom a close association between skeletal muscle mass and BMD is observed [12]. The relationship between skeletal muscle and bone can be explained by the Utah paradigm and the mechanostat hypothesis: bone growth and strength are influenced by mechanical load on bone, which regulates the processes of bone modelling and remodelling, and by other factors, such as hormones and micro-nutrients, which modulate these processes. Frost's mechanostat hypothesis proposes the mechanism by which the bone alters its architecture in

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response to mechanical loads induced by voluntary skeletal muscle contraction: mechanical loads cause bone strain, which triggers the remodelling of bone architectural adaptation [13,14]. Recent evidence supports this theoretical model [15,16], but the exact mechanisms behind changes in bone cell activity in response to mechanical stress are still under investigation. Of note, a reduction in osteocyte-dependent sclerostin secretion following muscle contraction induces new bone formation [17]. Patients with AN display higher level of sclerostin, parathyroid hormone and other markers of bone turnover compared with the general population [4].

There is a scarcity of evidence regarding skeletal muscle performance in patients with AN.

Muscle power has been shown to be positively associated with BMD [18] and may precede a decline in muscle strength and mass, as previously demonstrated in aging adults [19]. However, muscle power measurement requires highly specialized equipment and personnel, and is not easily implemented in a clinical setting. Thus, predictive equations for muscle power estimation have been developed from functional tests like the 5-repetition sit-to-stand test (5R-STS) and validated against reference methods [20].

This study aims at investigating the association between muscle power and BMD in patients with AN.

Methods

Study participants were enrolled according to the inclusion criteria: female sex, diagnosis of AN, age between 12 and 40 years. The exclusion criteria were the presence of any medical comorbidities influencing eating behaviour, physical functionality tests or BMD.

The clinical centres involved in the recruitment were the Department of Experimental Medicine and the Department of Human Neuroscience at Policlinico Umberto I – "Sapienza" University Hospital (Rome), and the Eating Disorders Clinic at the "Santa Maria Della Pietà" Hospital (Rome).

The study was approved by the local ethics committee, and written informed consent was provided by all participants or their parents or legal representatives.

All study participants underwent anthropometric assessment and body composition analysis. Body weight (to the nearest 0.1 kg) and height (to the nearest 0.1 cm) were measured using a mechanical column scale with a Seca stadiometer (Intermed SRL, Milan, Italy), according to standardized procedures [20], and body mass index (BMI) was calculated. For patients under 19 years of age, BMI Z-score and BMI percentiles were based on the World Health Organization charts [21]. Arm circumference (AC) was gathered with a measuring tape (to the nearest 0.1 cm). Skinfold thicknesses at different sites—triceps (TSF), biceps, subscapular, and suprailiac were assessed using a skinfold caliper (Harpenden, Baty International, UK); three measurements were taken and the mean value (to the nearest 0.1 mm) was computed for each site. Based on AC and TSF values, arm muscle area was calculated.

Physical activity level (PAL) was self-reported. In view of their clinical status, patients were instructed to avoid physical exercise and to limit physical activity to basic activities of daily living.

Physical functionality was evaluated through the 5R-STS. The time taken to complete the test was recorded, with a lower time indicating better performance [22]. Absolute and relative muscle power were calculated according to the predictive equation formulated by Alcazar *et al*. [20]:

- Lower-limb absolute muscle power = body weight x 0.9 x *g* x (height x 0.5 – chair height) / (time needed to complete 5R-STS / number of repetitions performed on the 5R-STS) x 5
- Lower-limb relative muscle power = 0.9 x *g* x (height x 0.5 – chair height) / (time needed to complete 5R-STS / number of repetitions performed on the 5R-STS) x 5

  where *g* (gravity) = 9.81 m/s^2.

Dual-energy X-ray absorptiometry scans were performed (Hologic Inc., Waltham, MA, USA) to estimate body fat percentage (%BF), appendicular lean mass (ALM) and femoral and lumbar BMDs.

Statistical analysis

Variables were checked for skewness and kurtosis. The collected data were expressed as mean ± standard deviation and as median and interquartile range for non-normally distributed variables. Between-group comparisons were performed using Student's t-test, with the exception of 5R-STS time and muscle power, where comparisons were adjusted for age using either a one-way ANCOVA (for parametric variables) or Quade's non-parametric ANCOVA (for non-parametric variables). Spearman's rho correlation coefficient was calculated to evaluate the association between BMD and functional measures. Multiple linear regression was used to explore the relationship between BMD and mean muscle power on the 5R-STS. Significance was set at $p < 0.05$. Statistical analysis was performed with SPSS Statistics, version 28 (IBM Corp., Armonk, NY, USA).

Results

Forty-four patients were enrolled (61% outpatients, 39% inpatients); participant characteristics are described in Table I.

Based on age, study participants were divided into two groups: the adolescent group (n=26) with median age 15.5 (14.75-17) years, mean BMI 15.5 ± 0.98 kg/m^2 and BMI Z-score -2.35 ± 0.52; and the adult group (n=18) with median age 23 (21-28) years and mean BMI 15.63 ± 1.21 kg/m^2 ($p>0.05$). The PAL of all patients was sedentary. Thirty-five out of forty-four patients (80%) had amenorrhea (92% in the adolescent group and 61% in the adult group), and nine patients (21%) had a regular menstrual cycle. Among the thirty-five amenorrheic participants, two had primary amenorrhea.

The time spent to complete the 5R-STS was similar between the adolescent group (12.10 ± 2.57 seconds) and the adult group (12.06 ± 3.52 seconds) ($p = 0.964$). The adolescent group exhibited mean absolute muscle power of 150 ± 41 watts (W) versus 145 ± 41 W in the adult patients, with no significant difference between the groups ($p = 0.664$).

No significant differences emerged between the two groups in BMD at lumbar or femoral level (Table II).

BMD values were correlated with 5R-STS scores and muscle power. A statistically significant positive correlation emerged between absolute muscle power and lumbar BMD (Spearman's rho = 0.323; p = 0.033) (Figure 1); a trend emerged between lower-limb relative muscle power and lumbar BMD (Spearman's rho = 0.280; p = 0.066) (Figure 2).

Multiple linear regression was performed to evaluate associations between lumbar BMD and lower- limb muscle power after adjusting for age, %BF and ALM. The detailed results of the regression models are shown in Table III. A significant positive association between lumbar BMD and lower-limb absolute muscle power emerged, even after adjustment for ALM (p = 0.006; SEE = 37.12). Age did not show a significant effect when included as a predictor. There was no significant association between lower-limb absolute muscle power and total femur BMD (p = 0.051; SEE = 39.62) or femoral neck BMD (p = 0.299; SEE = 40.95).

No associations between lower-limb relative muscle power and lumbar BMD emerged after adjusting for %BF (p = 0.051; SEE = 0.77) and ALM (p = 0.088; SEE = 0.78); similarly, no significant associations appeared between lower-limb relative muscle power and lumbar BMD after adjusting for both age and %BF (p = 0.117; SEE = 0.78) or age and ALM (p = 0.173; SEE = 0.79). After replacing lumbar BMD with either proximal femur BMD or femoral neck BMD, no associations emerged with relative 5R-STS muscle power (data not shown).

Table I Characteristics of study participants.

	PATIENTS WITH AN AGED ≤ 18 YEARS (N=26)	PATIENTS WITH AN AGED >18 YEARS (N=18)	*P*-VALUE
Age (years)	15.5 (14.7-17) [a]	23 (21-28) [a]	<0.001
Duration of illness (years)	1 (0.8-2) [a] (n=24)	3.5 (0.8-9.2) [a]	0.078
BMI (kg/m^2)	15.5 ± 1.0 [b]	15.6 ± 1.2 [b]	0.701
BMI Z-score	-2.3 ± 0.5 [b]	NA	NA
BMI percentile	1.7 ± 1.1 [b]	NA	NA
Triceps skinfold (mm)	8.2 ± 2.9 [b]	6.3 ± 3.2 [b]	0.049
Biceps skinfold (mm)	4.1 ± 1.1 [b]	3.6 ± 1.5 [b] (n=17)	0.157
Subscapular skinfold (mm)	6.3 ± 1.7 [b]	5.3 ± 1.7 [b] (n=17)	0.438
Suprailiac skinfold (mm)	5.5 ± 1.8 [b]	5.1 ± 3.1 [b] (n=17)	0.556
Arm circumference (cm)	20.3 ± 1.3 [b]	19.67 ± 1.4 [b]	0.433
Arm muscle area (cm^2)	25.1 ± 3.3 [b]	26.07 ± 4.1 [b] (n=17)	0.394
Body fat (%)	16.8 ± 3.5 [b]	16.30 ± 5.4 [b]	0.701
Appendicular lean mass (kg)	15.2 (13.6-16.8) [a]	15.5 (14.4-15.9) [a]	0.555
5R-STS (seconds) [§]	12.1 ± 2.6 [b]	12.1 ± 3.5 [b]	0.97°
5R-STS (score)	3.1 ± 0.9 [b]	3.22 ± 1.1 [b]	0.373°
Absolute 5R-STS muscle power (W)[§]	145.4 (124.7-170.1) [a]	133.3 (113.9-179.4) [a]	0.367°
Relative 5R-STS muscle power (m^2/s^3)	3.63 (3.1-4.2) [a]	3.69 (2.7-4.2) [a]	0.676°

5R-STS = 5-repetition sit-to-stand test; **BMI** = body mass index; **a** = results expressed as mean ± standard deviation (SD); **b** = results expressed as median and interquartile range; **§** = log-transformed variable; **°** = age-adjusted *p*-value.

Table II Lumbar spine, total femur and femoral neck bone mineral density.

		PATIENTS WITH AN AGED ≤ 18 YEARS	PATIENTS WITH AN AGED >18 YEARS	*P*-VALUE
L1-L4	Z-score	-1.23 ± 1.1 [a]	-1.56 ± 0.99 [a]	0.471 °
Femoral neck	Z-score	-1.1 (-1.85 - -0.075) [b]	-1.35 (-1.8 - -0.7) [b]	0.671 °
Total femur	Z-score	-1.07 ± 0.67 [a]	-0.93 ± 0.95 [a]	0.546 °

AN = anorexia nervosa; **a** = results expressed as mean ± standard deviation (SD); **b** = results expressed as median and interquartile range; ° age-adjusted p-value

Figure 1 Relationship between lumbar BMD and absolute 5R-STS muscle power. A positive correlation between absolute 5R-STS muscle and lumbar BMD was observed (**BMD** = bone mineral density; **5R-STS** = 5-Repetition Sit-To-Stand test).

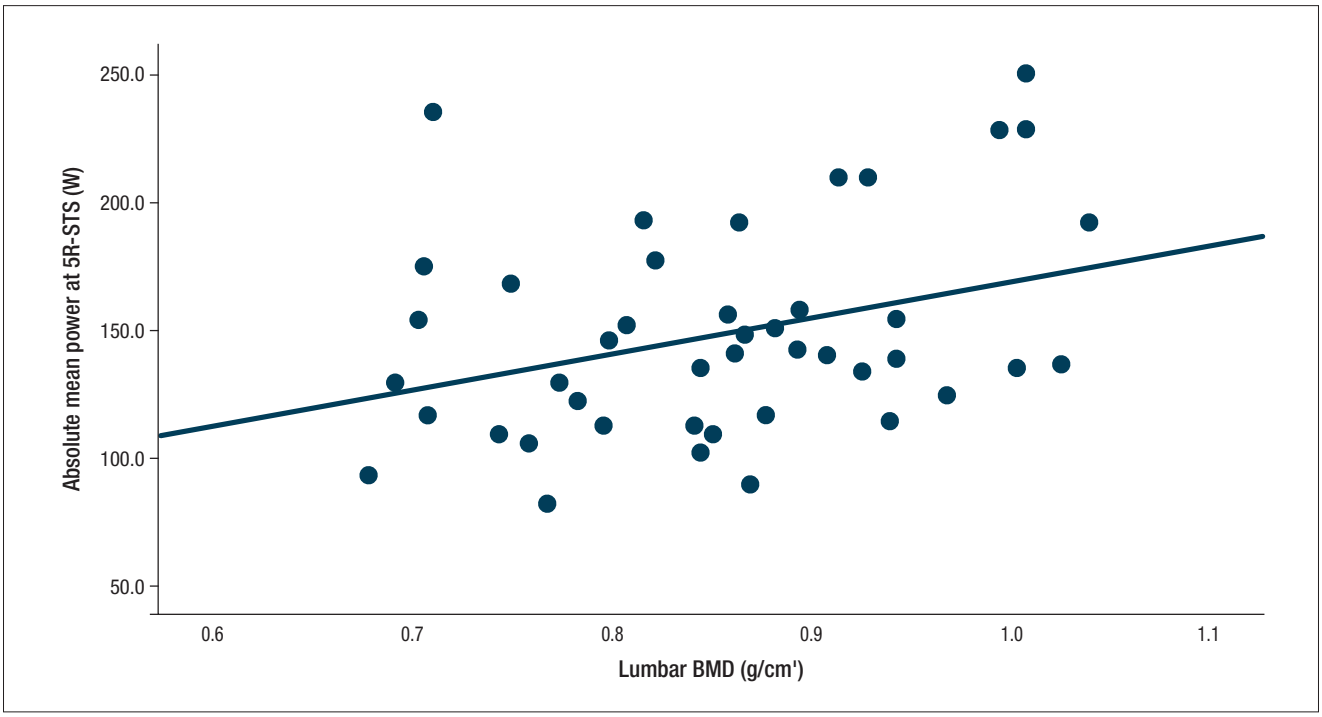
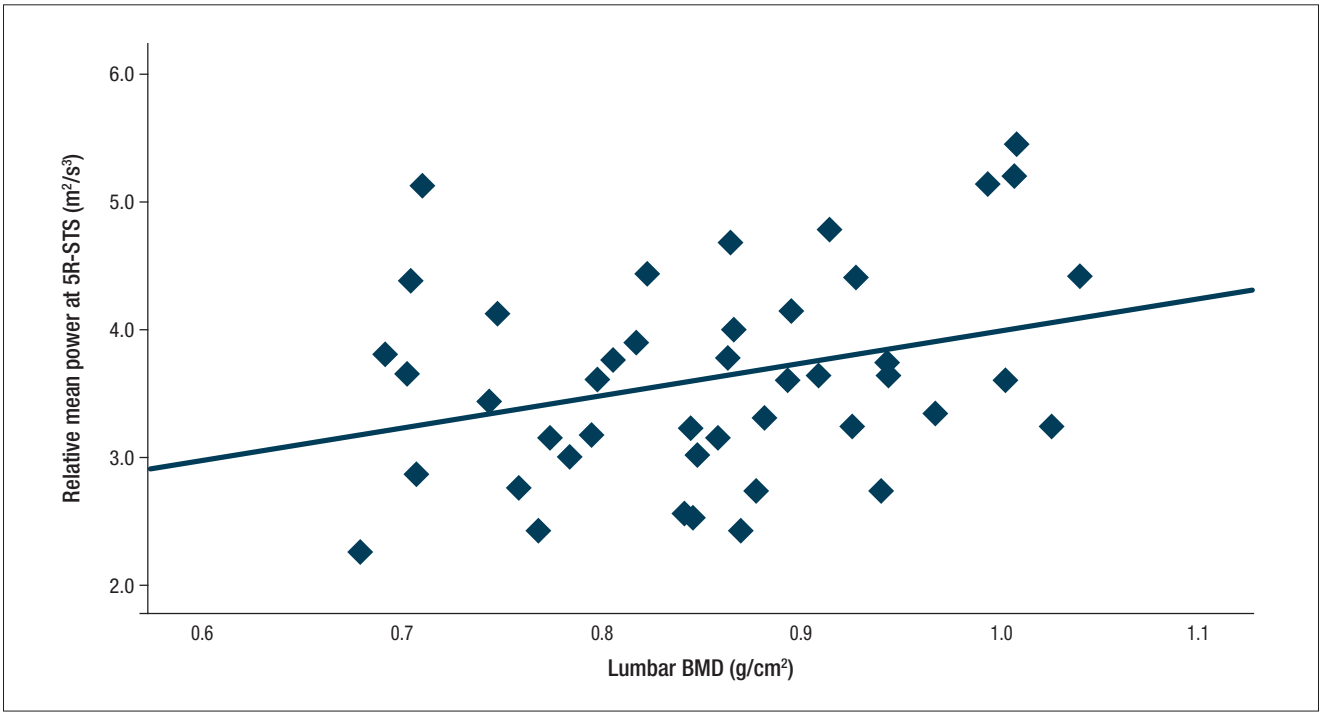


Figure 2 Relationship between lumbar BMD and relative 5R-STS muscle power. A positive trend between relative 5R-STS muscle power and lumbar BMD was observed (**BMD** = bone mineral density; **5R-STS** = 5-repetition sit-to-stand test).



Discussion and conclusions

The present study explored the impact of malnutrition on physical functionality, focusing on skeletal muscle power in the context of anorexia nervosa.

The mean score obtained on the 5R-STS was considerably lower than the average of the healthy population of the same age, according to reference values for age proposed by Bohannon [23]. However, no differences in BMD Z-scores and 5R-STS scores between adolescent and adult groups emerged.

Current evidence supports the concept that chronic low energy availability induces widespread endocrine dysfunction, including disruption of the muscle-bone unit. Previous studies

Table III Multiple linear regression predicted absolute mean power on the 5R-STS.

	UNSTANDARDIZED COEFFICIENT		STANDARDIZED COEFFICIENT β	T	SIG.	95% CONFIDENCE INTERVAL OF B	
	B	Standard error				Lower Bound	Upper Bound
MODEL 1							
Constant	-61.480	62.548		-0.983	0.331	-187.798	64.837
BMD (L1-L4)	121.273	58.014	0.292	2.090	0.043	4.111	238.436
ALM	7.021	3.024	0.324	2.322	0.025	0.915	13.127
MODEL 2							
Constant	5.980	52.388		0.114	0.910	-99.819	111.780
BMD (L1-L4)	122.309	60.094	0.294	2.035	0.048	0.946	243.672
%BF	2.289	1.362	0.243	1.681	0.100	-0.461	5.038

Dependent variable = absolute mean power on the 5R-STS; **5R-STS** = 5-repetition sit-to-stand test; **ALM** = appendicular lean mass; **%BF** = body fat percentage; **BMD** = bone mineral density.

on body composition in AN revealed reduced skeletal muscle mass and strength, which did not fully recover after weight restoration [24], as a result of a long-term negative energy balance. Since nutrients are primarily used to support visceral organ function, a reduced muscle mass secondary to decreased muscle protein synthesis (which itself carries a high metabolic cost) lowers resting metabolic rate [24]. Altered hormone levels and low body weight play a major role in bone microarchitecture changes [25,26]. Indeed, downregulation of the hypothalamic-pituitary-gonadal axis leads to low plasma oestrogen levels, contributing to increased bone reabsorption and decreased bone synthesis in AN, with involvement of the endocortical, intracortical and trabecular areas [27]. Hypercortisolaemia secondary to increased cortisol secretion and decreased renal clearance is frequently observed in patients with AN, diminishing bone formation and promoting bone reabsorption [28]. Previous evidence confirmed the association between undernutrition and low BMD [25,29,31]. Nevertheless, decreased lumbar BMD has been observed in normal-weight patients with bulimia nervosa, suggesting that low weight is not the sole contributing factor to reduced BMD; for instance, suboptimal intake of vitamin D, calcium and phosphorus can also play a role [32].

BMD is significantly associated with muscle strength, but the relationship between BMD and muscle power seems to be largely unexplored.

Several studies investigated muscle power across different populations. In the elderly, 5R-STS muscle power equations were employed to assess body and cognitive function, showing higher reliability than the 5R-STS score [20]. Conversely, the 5R-STS score correlates better with perceived health-related quality of life (HRQoL), suggesting that time taken to perform a daily activity, like standing up from a chair, influences perceived HRQoL more than muscle power. Findings from a paediatric population showed that underweight children had significantly lower muscle power than normal-weight peers [33]. In a cohort of healthy females aged 18 to 35 years, maximum muscle power evaluated using the Sargent test was significantly associated with total body BMD, total femur BMD and femoral neck BMD [34].

In our study, a positive association was found between BMD and muscle power but not with muscle mass, which may indicate that skeletal muscle mass deterioration follows muscle power decline.

After adjusting for age, the association between muscle power and BMD was no longer observed. Our data are in line with existing evidence showing that BMD was not dependent on age, while bone mineral content displayed a strong correlation with skeletal muscle development [14].

No association was found with femoral BMD: this observation could be attributed to a peculiar pattern of bone metabolism derangement. Indeed, patients with AN may experience an early increase in bone remodelling at the lumbar site, which is comprised of mainly trabecular bone, unlike the femoral site (mainly cortical bone) [4,35,36].

Our findings are somewhat consistent with observations by Mueller *et al*., who pointed out that volumetric bone mineral content (assessed through peripheral quantitative computed tomography) at the tibia level was dependent on and adapted to muscle forces after long-term (approximately three decades) recovery from AN [37]. The present study has some limitations. First, the small sample size may prevent generalizability of the results. Second, data on hormone levels, osteocalcin levels, and calcium and vitamin D supplementations were not available. Finally, the formula used to calculate muscle power was validated in an elderly population rather than in patients with AN; however, both populations exhibit similar impairments of body function and muscle strength.

Our results emphasize the relationship between lower-limb muscle power and lumbar BMD; this association is not fully explained by ALM. Sit-to-stand muscle power equations are readily applicable to clinical settings, since they require neither expensive devices nor highly-specialized personnel. Therefore, in the context of AN multidimensional assessment, muscle power estimation can aid in capturing detrimental changes of the muscle-bone unit, a necessary prerequisite for therapies targeted at BMD and muscle function recovery.

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