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Brain-Derived Neurotrophic Factor Is Related with Sarcopenia in Patients with Disease-Related Malnutrition

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Keywords
Brain-derived neurotrophic factor · Disease-related malnutrition · Sarcopenia · Ultrasound

Abstract

Introduction: Sarcopenia is a condition characterized by muscle mass loss. Some investigations have demonstrated the role of brain-derived neurotrophic factor (BDNF) as a protector against the presence of sarcopenia in patients with chronic kidney disease. We aimed to explore the role of circulating BDNF in the development of sarcopenia among individuals with disease-related malnutrition (DRM). ***Materials and Methods:*** A total of 160 patients diagnosed with DRM according to the Global Leadership Initiative on Malnutrition (GLIM) criteria were enrolled. Anthropometric data, muscle mass assessed via ultrasound at the rectus femoris quadriceps (RFQ) level, bioelectrical impedance analysis (skeletal muscle mass [SMM], appendicular skeletal muscle mass [aSMM], and appendicular skeletal muscle mass index [aSMMI]), handgrip strength, biochemical parameters, dietary intake, and circulating levels of BDNF were measured. ***Results:*** A total of 55 patients (34.4%) were classified as sarcopenic, while 105 patients (65.6%) were classified as non-sarcopenic. Phase angle (−0.6 ± 0.2°; p = 0.01), reactance (−5.8 ± 2.1 Ohms; p = 0.03), SMM (−3.3 ± 0.2 kg; p = 0.04), aSMM (−2.1 ± 0.3 kg; p = 0.03), aSMMI (−0.8 ± 0.2 kg; p = 0.03), dominant muscle area (−0.7 ± 0.2 cm^2; p = 0.04), and dominant Y-axis thickness (−0.4 ± 0.1 cm; p = 0.03) were worse in patients with sarcopenia. Muscle strength was higher in non-sarcopenic patients (8.5 ± 1.2 kg; p = 0.01). Circulating BDNF levels were significantly higher in non-sarcopenic patients compared to sarcopenic patients (94.7 ± 3.9 ng/mL; p = 0.01). Logistic regression analysis indicated a reduced risk of sarcopenia (OR = 0.16, 95% CI = 0.11–0.43; p = 0.03) in patients with higher BDNF levels, after adjusting for body mass index, gender, energy intake, and age. ***Conclusion:*** Our study identified an association between low serum BDNF levels and sarcopenia in patients with DRM.

Introduction

Sarcopenia is a syndrome defined by an age-related decline in skeletal muscle, leading to physiological and clinical consequences. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) established a definition of sarcopenia as the progressive and widespread reduction of skeletal muscle mass (SMM) and strength, associated with an increased risk of adverse outcomes such as physical disability, diminished quality of life, and mortality. They further recommended that sarcopenia diagnosis should be based on the coexistence

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of both low muscle mass and impaired muscle function [1]. In 2018, the EWGSOP revised its consensus (EWGSOP2), emphasizing that sarcopenia can also arise secondary to systemic diseases occurring earlier in life, particularly those that promote inflammatory processes, physical inactivity, or insufficient energy or protein intake [2]. Moreover, disease-related malnutrition (DRM) is associated with the patient's inflammatory status, disease-related alterations, reduced dietary intake, and decreases in body weight and muscle mass, too. Within this context, sarcopenia is, as abovementioned; a condition defined by reduced muscle mass, muscle weakness, and diminished functional capacity [2]. These characteristics contribute to significant health risks, including an increased likelihood of fractures, falls [3], and comorbid conditions [4]. Given this scenario, skeletal muscle represents the primary protein reservoir in the human body, and its mass is a key parameter for assessing DRM. Additionally, skeletal muscle has the ability to produce and secrete various molecules, collectively referred to as myokines, which facilitate communication with other tissues through endocrine, paracrine, or autocrine signalling [5].

Brain-derived neurotrophic factor (BDNF) belongs to the nerve growth factor family and mediates its effects by binding to the tropomyosin receptor kinase B receptor and it is considered a myokine, too. Among neurotrophins, BDNF is the most prevalent and widely distributed within the central nervous system. It is a basic dimeric protein with each subunit consisting of a 13.5 kDa molecule containing 119 amino acids. BDNF is a critical regulator of neuronal activity and synaptic plasticity in both the central and peripheral nervous systems, promoting the growth and maintenance of various neuronal systems by acting as a neurotransmitter modulator [6]. It is well established that BDNF expression increases in response to central nervous system insults. While numerous studies have highlighted BDNF's significant role in neuroprotection, recent evidence indicates that alterations in plasma BDNF levels, independent of the nervous system, are also linked to sarcopenia and metabolic disorders [7–9]. Some studies in the literature have demonstrated the role of BDNF as a protector against the presence of sarcopenia [10, 11], but these studies have been carried out only in patients with chronic kidney disease or kidney transplant. On the other hand, this relationship has not been demonstrated in other investigations [12, 13], but we must take into account that in none of the studies was the nutritional status or the presence of DRM assessed, and as we have previously commented, there is a close relationship between DRM and sarcopenia. Considering the few studies in the literature regarding BDNF with sarcopenia, the absence of studies in patients with malnutrition, and the relevant role of muscle in patients with DRM, we aimed to explore the role of circulating BDNF in the development of sarcopenia among individuals with DRM, a population characterized by a high prevalence of sarcopenia.

Materials and Methods

Study Population

This open-label, real-world study involved outpatients diagnosed with DRM. These patients were referred to our nutrition unit for a nutritional assessment due to a suspected risk of malnutrition, with recruitment taking place between January 2023 and July 2024. Nutritional status was assessed in all participants using anthropometric measurements and biochemical markers. Prior to participation, all individuals provided informed consent. The study protocol received approval from the Bioethical Committee of the Health Area of HCUVA (PI 20-2062) and adhered to the ethical principles outlined in the Declaration of Helsinki.

Inclusion criteria required participants to be over 60 years of age and diagnosed with DRM based on Global Leadership Initiative on Malnutrition (GLIM) criteria [14]. Exclusion criteria included chronic kidney disease, alcohol consumption, active cancer, decompensated liver disease, diabetes mellitus, fluid overload from decompensated cardiopulmonary disease inability to walk, or failure to provide informed consent.

In all these subjects, anthropometric composition analysis and blood sample collection were conducted during the same clinical appointment. During this visit, the following measurements were obtained: body weight, height, body mass index (BMI), and calf circumference. Additional evaluations included dynamometry, bioimpedance analysis (BIA), muscle mass measurement using ultrasound at the rectus femoris quadriceps (RFQ), and blood sample collection. For the biochemical assessments, 15 mL of venous blood were drawn into EDTA-coated tubes after a 10-h overnight fasting period. The parameters analysed included albumin (g/dL), C-reactive protein (mg/dL), prealbumin (mg/dL), along with serum levels of BDNF.

Anthropometric Measurements, Muscle Ultrasound, BIA, and Dietary Intake

Body weight was recorded with participants undressed, using a digital scale (Omron, LA, CA, USA). After this determination, height (cm) and waist circumference (cm)

were measured using a nonelastic tape measure (Omron, LA, CA, USA). BMI was then calculated as body weight (kg) divided by the square of height (m^2). Calf circumference was assessed at the widest part of the gastrocnemius muscle using a tape measure. BIA was employed to determine the components of impedance (Z), including resistance (R) and reactance (X). The phase angle (PhA) was calculated with the formula: PhA = (X/R) × (180°/π). BIA provided estimates of fat mass (FM), SMM, appendicular skeletal muscle mass (aSMM), and appendicular skeletal muscle mass index (aSMMI), which was calculated as aSMM divided by height squared [15] (EFG BIA 101 Anniversary, Akern, Italy).

Muscle ultrasound was used to evaluate the RFQ in the dominant lower extremity. A 10- to 12-MHz multifrequency linear probe (Mindray Z60, Madrid, Spain) was utilized, aligned perpendicularly to the longitudinal and transverse axes of the RFQ. Measurements were taken without applying pressure, at the distal third between the superior patella pole and the anterior superior iliac spine. The parameters recorded included the cross-sectional area (cm^2), circumference (cm), X-axis diameter (cm), Y-axis diameter (cm), and the X/Y ratio of the RFQ [16].

Handgrip strength was measured using a dynamometer (JAMAR®, Sammons Preston, Bolingbrook, IL, USA) with participants seated and their arm at a right angle to the forearm. Three trials were conducted, and the average was calculated. Muscle strength was classified as low according EWGSOP2 criteria, defined as <27 kg for men and <16 kg for women [2]. Confirmed sarcopenia was diagnosed when low muscle strength was accompanied by a reduced aSMMI based on BIA values (<7.0 kg/m^2 for men and <5.5 kg/m^2 for women) [2].

Finally, all participants were instructed to document their daily dietary intake over three nonconsecutive days, including 2 weekdays and 1 weekend day. Dietary records were analysed using specialized software (DietSource®, Geneva, Switzerland) with national food composition tables as a reference [17]. Additionally, patients recorded the duration of their daily physical activity in a dedicated diary.

Biochemistry

Nutritional parameters were assessed using a Cobas c-711 autoanalyzer (Roche Diagnostics, Geneva, Switzerland) to measure albumin (g/dL), C-reactive protein (mg/dL), and prealbumin (mg/dL). BDNF were determined using the MILLIPLEX® Human Myokine Magnetic Bead Panel (HCYTOMAG-56K, EMD Millipore Corporation, MA, USA), following the manufacturer's guidelines. The inter-assay coefficient of variation for BDNF was 2.5%, while the intra-assay coefficient of variation was 3.0%.

Statistical Analysis

Statistical analyses were conducted using SPSS statistical software for Windows, version 23.0 (SPSS Inc., Chicago, IL, USA). The sample size was calculated to detect differences of 10 ng/mL in circulating BDNF between DRM patient groups (with and without sarcopenia). The normality of the variables was assessed using the Kolmogorov test. Descriptive statistics are presented as mean ± standard deviation for continuous variables and as percentages for categorical variables. Variables with a normal distribution were analysed using the Student's *t* test. To minimize the risk of type I error in association analyses, the Bonferroni correction was applied for multiple comparisons. Qualitative variables were analysed using the chi-square test. Multiple logistic regression models were employed to calculate odds ratios (ORs) and 95% confidence intervals (CIs), examining the association between BDNF levels and the presence of sarcopenia (median level: 14.17 ng/mL). Statistical significance was set at a p value <0.05.

Results

160 patients with DRM, as defined by the GLIM criteria, were enrolled in the study, with a mean age of 64.2 ± 1.5 years. The cohort consisted of 87 females (54.4%) and 73 males (45.6%). The underlying causes of DRM were distributed as follow: stable oncological conditions in 85 patients (52.8%), gastrointestinal diseases in 36 patients (22.4%), cardiopulmonary diseases in 21 patients (13.0%), and miscellaneous causes in 18 patients. This distribution reflects a representative sample of DRM patients typically seen in our clinical unit.

Table 1 summarizes the anthropometric, muscle ultrasound, bioimpedance, and biochemical characteristics of the study population, indicating that the mean BMI and body weight were within normal limits. A total of 55 patients (34.4%) were classified as sarcopenic based on the criteria established by the European Working Group on Sarcopenia in Older People (EWGSOP2) [2], while 105 patients (65.6%) were classified as non-sarcopenic (Table 2). The sex distribution was similar between the groups: in the sarcopenia group, there were 29 females (52.7%) and 26 males (47.3%), whereas in the non-sarcopenia group, there were 58 females (55.2%) and 47 males (44.8%).

Table 2 presents significant statistical differences in anthropometric parameters, including calf circumference (−1.1 ± 0.3 cm; $p = 0.02$). Bioimpedance parameters were also less favourable in patients with sarcopenia, as

Table 1. Epidemiological, anthropometric, and biochemical parameters of the total sample (mean ± SD)

Parameters	Total group, n = 160
Age, years	64.2±1.5
BMI, kg/m^2	23.3±5.1
Body weight, kg	58.9±16.7
Fat mass, kg	18.5±3.1
SMM, kg	20.0±1.3
aSMM, kg	16.5±2.1
aSMMI, kg	6.7±0.8
CC, cm	31.8±1.9
PhA (°)	5.1±0.4
Reactance, Ohms	51.0±4.1
Resistance, Ohms	580.1±24.1
Dominant muscle area RFQ, cm^2	3.2±1.1
Dominant circumference area RFQ, cm	8.2±1.4
Dominant X axis RFQ, cm	3.3±0.5
Dominant Y axis RFQ, cm	1.2±0.5
Dominant X/Y axis RFQ, cm	3.3±0.1
Dominant eco-intensity (points)	91.0±12.1
Strength, kg	21.4±3.2
CRP, mg/dL	7.8±2.1
Albumin, g/dL	4.7±3.0
Prealbumin, mg/mL	23.9±7.8
BDNF, ng/mL	157.1±4.6

CC, calf circumference; SMM, skeletal muscle mass; aSMM, appendicular skeletal muscle mass; aSMMI, appendicular skeletal muscle mass index; RFQ, rectus femoris quadriceps; CRP, C-reactive protein.

indicated by a lower PhA (−0.6 ± 0.2°; p = 0.01), reactance (−5.8 ± 2.1 Ohms; p = 0.03), SMM (−3.3 ± 0.2 kg; p = 0.04), aSMM (−2.1 ± 0.3 kg; p = 0.03), and aSMMI (−0.8 ± 0.2 kg; p = 0.03). Furthermore, ultrasound parameters for RFQ were worse in sarcopenic patients, with reductions in dominant muscle area (−0.7 ± 0.2 cm^2; p = 0.04), dominant Y-axis thickness (−0.4 ± 0.1 cm; p = 0.03), and an increased dominant X/Y axis ratio (0.7 ± 0.3; p = 0.04). Finally, muscle strength was higher in non-sarcopenic patients (8.5 ± 1.2 kg; p = 0.01).

Table 2 also includes biochemical parameters. Patients with sarcopenia exhibited lower serum protein levels, including albumin (−0.5 ± 0.1 g/dL; p = 0.04) and prealbumin (−7.8 ± 0.7 mg/dL; p = 0.02). Circulating BDNF levels were significantly higher in non-sarcopenic patients compared to sarcopenic patients (94.7 ± 3.9 ng/mL; p = 0.01). When stratified by dynapenia (defined as low strength based on EWGSOP2 criteria: <27 kg in males and <16 kg in females [2]), patients with low strength demonstrated significantly lower BDNF levels (194.1 ± 8.3 pg/mL vs. 120.7 ± 7.2 pg/mL; p = 0.01) compared to those with normal strength (>27 kg in males and >16 kg in females).

Table 3 summarizes dietary intakes and physical activity levels. The daily minutes of physical activity were lower in subjects with sarcopenia (40.3 ± 8.2 min/week; p = 0.01). Moreover, energy intake, as well as carbohydrate, fat, and protein consumption were lower in patients with sarcopenia compared to those without sarcopenia.

Correlation analysis revealed a significant positive relationship between BDNF levels and several ultrasound parameters of rectus femoris quality (RFQ), including dominant muscle area, dominant circumference, and

Table 2. Comparison of epidemiological, anthropometric, and biochemical parameters between patients with and without sarcopenia (mean ± SD)

Parameters	No sarcopenia, $n = 105$	Sarcopenia, $n = 55$	p value
Age, years	64.1±2.1	64.9±1.4	0.23
BMI, kg/m^2	23.7±2.1	23.2±1.1	0.21
Weight, kg	61.1±5.9	57.1±3.1	0.11
Fat mass, kg	19.7±3.0	18.5±2.3	0.13
Skeletal muscle mass, kg	21.8±1.4	18.5±1.0	0.04
Appendicular muscle mass (aSMM)	17.5±1.2	15.4±1.0	0.03
Appendicular muscle mass index (aSMMI)	7.0±0.3	6.1±0.4	0.03
CC, cm	32.2±1.0	31.0±0.9	0.02
PhA (°)	5.3±0.2	4.7±0.3	0.01
Reactance, Ohms	54.1±2.0	47.7±2.1	0.03
Resistance, Ohms	590.7±44.1	566.3±51.2	0.07
Dominant muscle area RFQ, cm^2	3.4±0.2	2.7±0.3	0.04
Dominant circumference RFQ, cm	8.4±1.1	8.1±1.0	0.21
Dominant X axis RFQ, cm	3.3±0.4	3.2±0.2	0.39
Dominant Y axis RFQ, cm	1.3±0.1	0.9±0.1	0.03
Dominant X/Y axis RFQ, cm	3.2±0.2	3.9±0.2	0.04
Dominant eco-intensity (points)	90.5±14.1	92.3±11.1	0.23
Strength, kg	25.4±3.0	16.9±3.0	0.01
CRP, mg/dL	6.6±2.2	8.3±3.2	0.38
Albumin, g/dL	4.8±0.3	4.3±0.6	0.04
Prealbumin, mg/mL	27.7±2.1	19.9±2.1	0.02
BDNF, ng/mL	189.2±4.3	99.5±3.2	0.01

CC, calf circumference; SMM, skeletal muscle mass; aSMM, appendicular skeletal muscle mass; aSMMI, appendicular skeletal muscle mass index; RFQ, rectus femoris quadriceps.

Table 3. Comparison of baseline characteristics, average daily intakes, and physical activity between patients with and without sarcopenia (mean ± SD)

Parameters	Total group, $n = 160$	No sarcopenia, $n = 105$	Sarcopenia, $n = 55$	p value
Calorie intake, kcal/day	1,595.3±313.2	1,634.1±212.1	1,466.1±203.2	$p = 0.01$
Carbohydrate intake, g/day (PTC)	168.7±51.1 (43.2%)	170.3±57.1 (43.2%)	153.2±29.1 (42.3%)	$p = 0.02$
Fat intake, g/day (PTC)	68.3±12.1 (39.1%)	71.9±11.2 (39.7%)	61.8±8.9 (38.8%)	$p = 0.02$
Protein intake, g/day (PTC)	69.3±9.1 (18.6%)	70.7±5.1 (17.1%)	67.2±3.1 (19.9%)	$p = 0.02$
Fibre intake, g/day	13.5±5.0	13.6±4.1	13.3±4.2	$p = 0.31$
Physical activity, min/day	77.3±8.2	89.2±4.8	49.3±3.2	$p = 0.01$

PTC, percentage of total calorie.

Table 4. Correlation analysis between BDNF and other variables

Parameters	BDNF
Dominant muscle area RFQ, cm^2	$r = 0.22$, $p = 0.02$
Dominant circumference RFQ, cm	$r = 0.25$, $p = 0.01$
Dominant Y axis RFQ, cm	$r = 0.27$, $p = 0.02$
aSMMI, kg/m^2	*r= 0.12, p = 0.04*
PhA, UI/L	$r = 0.23$, $p = 0.03$
Reactance, Ohms	$r = 0.21$, $p = 0.02$
Strength, kg	$r = 0.24$, $p = 0.03$

SMM, skeletal muscle mass; aSMM, appendicular skeletal muscle mass; aSMMI, appendicular skeletal muscle mass index; RFQ, rectus femoris quadriceps.

dominant Y-axis thickness, as well as raw bioimpedance parameters (PhA and reactance) (Table 4). In contrast, only aSMMI values as indirect SMM by bioimpedance correlated with BDNF, and there were no correlations with intake values or with the time of weekly physical activity.

Based on the preceding data, patients were divided into two groups according to the median BDNF value (141.7 ng/mL), and the OR for the risk of developing sarcopenia was calculated. Patients with BDNF levels above the median cutoff point had a significantly lower risk of sarcopenia compared to those below the cutoff (OR = 0.14, 95% CI = 0.07–0.30; $p = 0.01$). Furthermore, logistic regression analysis indicated a reduced risk of sarcopenia (OR = 0.16, 95% CI = 0.11–0.43; $p = 0.03$) in patients with higher BDNF levels, treated as a dichotomous parameter, after adjusting for BMI, gender, energy intake, and age.

Discussion

Our study demonstrated an inverse association between circulating BDNF levels and sarcopenia in patients with DRM. In this population, BDNF levels were significantly lower in individuals with sarcopenia. This relationship between circulating BDNF and sarcopenia risk remained statistically significant even after adjusting for potential confounding factors in the logistic regression model.

BDNF, a neurotrophic family protein, is essential for several biological processes, including neuronal and glial development, synaptic function, and neuroprotection [17]. Additionally, BDNF supports synaptic enhancement at neuromuscular junctions [18], aids motor neuron survival [19], and contributes to muscle growth and metabolic processes [20]. BDNF is widely distributed throughout the brain and detectable in plasma, too. While skeletal muscles in humans and rodents produce and secrete BDNF in response to physical activity, this muscle-derived BDNF is believed to function locally through autocrine and paracrine mechanisms, facilitating muscle fat metabolism and possibly influencing muscle development [21]. The primary source of circulating BDNF, however, is megakaryocytes [22]. Physical exercise stimulates platelet activation, which triggers the release of BDNF into the bloodstream [23]. In our present study, we found that plasma BDNF levels were significantly reduced in patients with sarcopenia. Moreover, BDNF levels were positive correlated with muscle strength by dynamometry. Miyazaki et al. [10] demonstrated similar results in patients with chronic kidney disease and haemodialysis, with a correlation between low BDNF values and physical function tests such as 6-m walk and 5-time chair stand test. The hypothesis of these authors to explain this association is the presence of an inflammatory situation that decreases the production of BDNF in muscle and megakaryocytes. This situation may be similar to that present in our patients with DRM, which is characterized by an inflammatory situation [14].

In another study, this time also with chronic kidney disease, specifically with kidney transplants [11], the group of patients with low skeletal muscle mass index (SMI) exhibited significantly reduced serum BDNF levels. Lower serum BDNF levels have been associated with exercise intolerance in patients with heart failure [24], while physical activity has been shown to increase BDNF levels [25]. However, other studies have shown an inverse relationship between circulating BDNF levels and sarcopenia in elderly South American females [12] and in Asian patients with chronic obstructive pulmonary disease [13]. These discrepancies may be due to different factors, such as ethnicity, different renal function of patients in these previous studies, and other unknown factors. Despite this, different scientific societies [26] are making clinical guidelines in which the usefulness of these serum markers to evaluate muscle health is indicated, including in these panels the serum levels of BDNF.

In our study, BDNF demonstrated a notable association with strength and muscle mass parameters, as assessed through ultrasound measurements of the RFQ and bioimpedance parameters, too. Furthermore, the relationship between muscle mass and BDNF levels across various parameters retained statistical significance in the

correlation analysis, and the association with strength was evident, too. This finding suggests that serum BDNF levels may be closely influenced by quantitative muscle parameters rather and functional ones [10].

The positive correlations between BDNF levels and ultrasound-derived measures of the RFQ suggest that higher circulating BDNF is associated with better preserved muscle architecture and volume. Clinically, these findings imply that BDNF may reflect not only the quantity but also the quality of muscle tissue in DRM patients.

PhA and reactance are indirect indicators of cellular integrity and body cell mass. The observed positive correlations between BDNF and these parameters suggest that higher BDNF levels are associated with better cell membrane integrity and higher muscle quality. This supports the hypothesis that BDNF may be a marker of overall muscle health and metabolic function [10].

In other hand, a relationship in the quality of the diet and BDNF has been demonstrated in patients with higher levels of BDNF [27]. In this previous study with a cluster analysis, cluster 1 had the tendency for the highest BDNF levels (of the best quality of diet) and a potential relationship between BDNF concentration and physical activity level was observed. Probably, in our study, the presence of patients with DRM does not allow us to find these relationships between BDNF levels and diet quality, taking into account the low protein caloric intake of this group. It has also been shown that BDNF appears to play an important role in the beneficial effects of exercise. Physical activity increases BDNF levels, and this increase occurs both with acute aerobic physical activity and with resistance exercise [25].

Our study has several limitations that warrant consideration. First, the study focused exclusively on patients with DRM, which constrains the generalizability of the results to broader populations. Second, the relatively small sample size may limit the robustness of the findings. Third, the cross-sectional design precludes establishing causal relationships between the studied variables. Despite these limitations, the study also possesses notable strengths. The inclusion of a wide range of DRM patients reflects the heterogeneity typically encountered in clinical practice. While this variability could be considered a limitation, it enhances the relevance of the findings to patients commonly seen in nutrition clinics. Additionally, it employed diverse methodologies to assess muscle mass, including BIA and ultrasound of the rectus femoris, both of which are noninvasive, free of ionizing radiation, and provide rapid assessments, making them highly practical. On the other hand, in our work, we examined the fluctuations in BDNF levels, which could have been seen in the work carried out in patients with haemodialysis. Lastly, dietary intake and physical activity were comprehensively evaluated, reducing the potential confounding effect of varying exercise levels on the observed outcomes.

While our cross-sectional design limits causal inference, further studies – particularly with longitudinal and interventional designs – are needed to elucidate whether BDNF has a mechanistic role in sarcopenia progression or is merely a downstream marker [10, 11]. Taking to account that circulating BDNF primarily reflects systemic activity and is largely released by platelets and megakaryocytes, whereas muscle-derived BDNF acts locally through autocrine and paracrine mechanisms. This local BDNF influences muscle metabolism and neuromuscular junctions without significantly contributing to serum levels, which instead serve as an indirect marker of overall muscle health. Finally, we could interpret higher serum BDNF levels in non-sarcopenic individuals as a multifactorial phenomenon, reflecting not only muscle quantity but also better neuromuscular integrity, lower inflammation, and more preserved platelet function.

In conclusion, our study identified a strong association between low serum BDNF levels and sarcopenia in patients with DRM. These findings suggest that serum BDNF may serve as a valuable biomarker for the diagnosis or as a potential target for novel therapeutic approaches in managing sarcopenia among DRM patients.

Statement of Ethics

This study protocol was reviewed and approved by the HCUVA Committee, Approval No. [PI20/2062] Written Informed consent was obtained from all individual participants included in the study. Signed informed consent was obtained in all participants. This research complies with the guidelines for human studies in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Daniel de Luis designed the study and wrote the article. Juan Jose Lopez Gomez and Olatz Izaola realized nutritional evaluation. David Primo and Daniel de Luis realized biochemical evaluation.

Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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