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INFLUENCE OF FAT AND FAT-FREE MASS ON THE PHASE ANGLE OF PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

INFLUÊNCIA DA MASSA MAGRA E GORDA NO ÂNGULO DE FASE DE PACIENTES COM DISTROFIA MUSCULAR DE DUCHENNE

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ABSTRACT: Objective: To realize a narrative review of the literature to explore aspects related to the percentage of lean fat mass (FM) and fat-free mass (FFM) and their relationship with phase angle (PA) in patients with Duchenne muscular dystrophy (DMD). **Methods:** A literature review was carried out, through a search in health science databases, using the terms Duchenne Muscular Dystrophy; Bioelectrical Impedance, Body Composition. **Results:** 9 studies met the selection criteria and were included in this review. The data indicate that individuals with DMD have a higher percentage of FM, a lower percentage of FFM and lower PA values than healthy subjects, where the absence of dystrophin results in instability in the muscle membrane and a subsequent decrease in PA. **Conclusion:**The FFM, MG and AF variables are modified with the progression of DMD, and the relationship between them is not clear. It is suggested that future studies explore the prognostic and therapeutic potential of the use of PA in DMD, correlating it with measures of functional performance and muscle strength.

KEYWORDS: Duchenne muscular dystrophy; Body Composition; Bioelectrical Impedance; Dystrophyn; phase angle.

RESUMO: Objetivo: realizar uma revisão narrativa de literatura a fim de explorar aspectos relacionados ao percentual de massa magra gorda (MG) e de massa livre de gordura (MLG) e sua relação com os valores do ângulo de fase (AF) em pacientes com Distrofia muscular de Duchenne (DMD). **Métodos:** Foi realizada uma revisão narrativa da literatura, com busca em bancos de dados de ciências da saúde, utilizando os termos Duchenne Muscular Dystrophy; BioelectricalImpedance, Body Composition. **Resultados:** A análise dos nove estudos inseridos mostrou que indivíduos com DMD apresentam maior porcentagem de MG, menor porcentagem de MLG e valores de AF inferiores à indivíduos saudáveis. A ausência de distrofina resulta em instabilidade na membrana muscular e consequentemente, redução do AF. **Conclusão:** As variáveis de MLG, MG e AF são modificadas com a progressão da DMD, não estando clara a relação entre elas. Sugere-se que futuros estudos explorem o potencial prognóstico e terapêutico do uso do AF na DMD, correlacionando-o com medidas de desempenho funcional e força muscular.

PALAVRAS-CHAVE: Ângulo de fase. Composição Corporal. Distrofia muscular de Duchenne. Distrofina. Impedância Bioelétrica.

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INTRODUCTION

Duchenne Muscular Dystrophy (DMD) is a degenerative and progressive genetic disease characterized by the absence of dystrophin protein[1]. Dystrophin is a structural protein of the costamere and helps stabilize the sarcolemma during contractions and in situations of longitudinal stress, such as stretching[2]. The absence of dystrophin leads to loss of cell membrane integrity and consequent fiber degeneration, exhaustion of regenerative capacity, fibrosis and replacement of muscle tissue with fat[2]. Clinically, individuals with DMD have progressive muscle weakness, with loss of walking ability between 7 and 13 years and death in the second decade of life [3,4].

The progression of the disease can also be accompanied by a serious public health problem: obesity, which in this population is associated with continuous physical inactivity and the long-term use of corticosteroid therapy [3,5]. Around 50% of patients with DMD develop early obesity, which can contribute to the occurrence of obstructive sleep apnea and fractures, further impairing the quality of life in this population[5]. There should be a focus on improving the quality of the diet in early childhood as a strategy to prevent obesity and encourage healthy habits[5].

Some changes in the body composition of these patients have already been well outlined in the literature, such as a reduction in lean mass and an increase in fat mass[6]. In view of this, body composition analysis is an important component of the assessment of individuals with DMD, allowing the results of therapies aimed at preserving muscle mass and reducing the increase in adipose tissue to be analyzed[7]. Considering the irreversibility of DMD, it is essential to adopt assessment strategies that can identify early possible points of intervention to prevent complications and improve the quality of life of these patients.

Among the variables evaluated in body composition, phase angle (PA) is a measure that reflects the different electrical properties of body tissues and can indicate changes in the integrity of cell membranes [8,9]. Compared to healthy individuals, DMD patients often have a low PA, which is correlated with the severity of the disease [9,10]. The prognostic value of the PA has been shown in different health conditions, such as cancer[10]; stroke[11]; cardiovascular disease[12]; kidney failure[13]; Covid-19[14], amyotrophic lateral sclerosis[15], and systemic sclerosis[16]. With the progression of DMD, changes in body composition can lead to changes in the body's electrical conductivity which can be reflected in PA values [8,17,18].

Considering that in DMD there are cellular alterations related to the structural integrity of the costamere and changes in body composition, the aim of this study was to perform a narrative literature review to explore aspects related to the percentage of lean mass and fat-free mass and their relationship with PA values, considering the possible prognostic value of the PA.

METHODOLOGY

DATABASE SEARCH

Based on the question: “In DMD, is the clinical prognosis related to fat-free mass, fat mass and PA?”, a narrative literature review was performed by searching the health sciences databases PubMed, Latin American and Caribbean Center on Health Sciences Information (BIREME), Scielo, LILACS, Physiotherapy Evidence Data Base (PEDro), using the key-words: Duchenne Muscular Dystrophy; Bioelectrical Impedance, Body Composition.

The inclusion criteria were (1) the use of Bioelectrical Impedance Analysis (BIA) in individuals with DMD, (2) analysis of the PA and/or other body composition variables, (3) articles published in the last 20 years (2001 to 2021), in Portuguese or English. The exclusion criteria were: (1) not using BIA as a method of analyzing body composition, (2) studies carried out on animal models, (3) other myopathies without DMD in the sample, (4) studies with individuals with DMD, but without analysis of body composition and (5) studies in a form other than an article (theses, monographs and similar texts).

ARTICLES ANALYZES

The articles were analyzed regarding their aims, methods (study groups, evaluation methods) and results (results obtained with bioelectrical impedance analysis, comparison between groups, phase angle analysis).

RESULTS

ARTICLES SELECTION

A total of 67 potential studies published in the last 20 years (2001 to 2021) were identified. Initial analysis indicated that 32 studies were duplicates, 17 studies did not use BIA to assess body composition, five studies involved individuals with DMD but did not perform body composition analysis, three studies were conducted with animals and one study did not involve individuals with DMD (Figure 1).

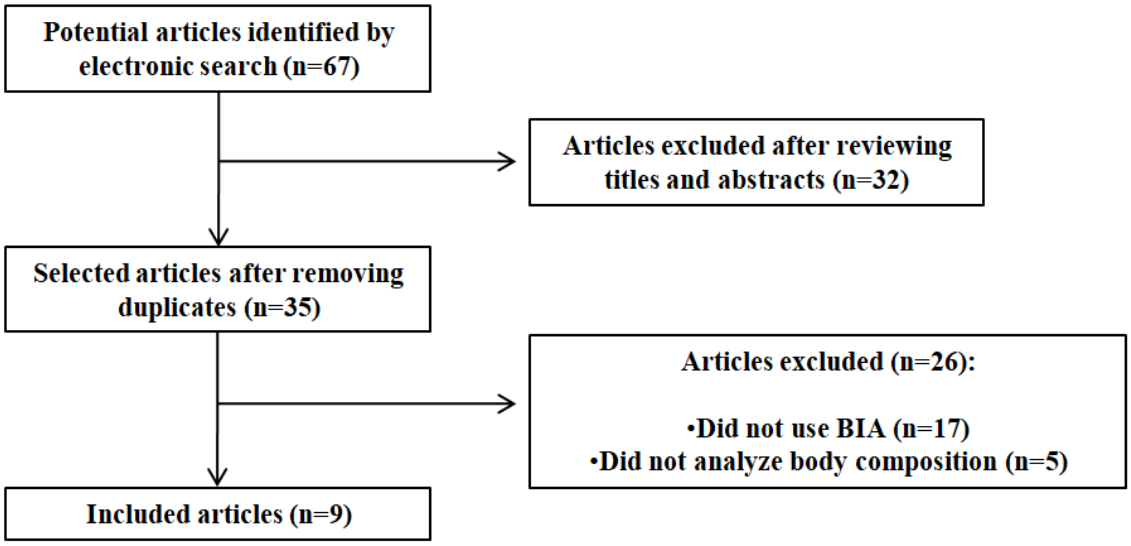

Figure 1: Flowchart for selecting articles. n: number of articles; BIA: electrical bioimpedance.

Therefore, nine studies met the inclusion criteria and were analyzed. The data obtained is described in Table 1.

Table 1: Summary of the articles included in the review

Article	Sample	Main results related to PA or other body composition variables
(MOK et al., 2006)[19]	11 patients with DMD (mean age 10.0 ± 2.5 years).	Some body composition assessment methods can overestimate FM and FFM in patients with DMD. BIA should be used in the assessment of DMD patients for early detection of fat accumulation. There was no analysis of PA.
(MOK et al., 2010)[10]	26 patients with DMD (ages between 3 and 11 years).	DMD patients had an average BMI of 15.4 Kg/cm2, with no obese patients. The % of FM increased with advancing age. There was no analysis of PA.
(JACQUES et al., 2018)[22]	76 participants (16 healthy and 50 with some form of muscular dystrophy).	Patients with dystrophy had more fat mass than healthy people (around 34-46%). DMD patients had less FFM than other types of dystrophy (around 21-28% less). There was no analysis of PA.
(SOUZA et al., 2014)[28]	3 patients with DMD (ages 6, 7 and 8).	The percentage of lean mass varied between 12 and 27.5% and fat mass between 72.5 and 89.5%. The % of fat mass increased with age. Older patients had lower MFM scores and higher energy expenditure. There was no analysis of PA.
(BARJA; PÉREZ, 2016)[20]	40 patients with muscular dystrophy (mean age 13.6 ± 3.3 years).	The conventional nutritional assessment overestimated the % of MG and underestimated the REE. The actual energy intake of dystrophy patients: 1452 (1033-2476) was higher than the recommended: 1300 (900-1900) kcal / day, p <0.001. There was no analysis of PA.
(SAURE et al., 2018)[23]	63 patients with DMD (ages between 5.4 and 18.7 years).	Wheelchair patients had a higher percentage of MG than ambulant patients (72% vs 46%, p <0.05).There was no analysis of PA.
(VERMEULEN et al., 2019)[8]	43 patients with DMD (ages between 2.7 and 19.8 years).	Patients with DMD had lower PA than the reference values.
(SOUZA et al., 2020)[6]	20 patients with DMD (aged between 4 and 12).	Patients with poorer performance in functional tests have lower phase angle values when compared to patients with better performance in functional tests.
(GRILO et al., 2020)[21]	46 patients with DMD (aged between 5 and 20).	BIA is a method capable of estimating the percentage of fat-free mass in patients with DMD. Patients had an average BMI of 17 Kg/cm2 and an average fat mass of 30% of body mass. There was no analysis of PA.

DMD: Duchenne muscular dystrophy. BIA: electrical bioimpedance. FFM: fat-free mass. FM: fat mass. PA: phase angle. % percentage. REE: resting energy expenditure. BMI: body mass index.

DESCRIPTIVE SYNTHESIS

Of the nine studies included in this narrative review, four[7,19-21] compared the BIA method with other methods such as skinfold thickness measurement (ST), labeled water dilution (WD) and dual-energy X-ray absorptiometry (DXA) for body composition assessment, estimating the % of FFM and FM in patients with DMD and demonstrating that BIA is a valid, accessible and inexpensive method for the assessment and clinical management of patients.

One of the studies showed that DMD patients have a lower percentage of FFM than patients with other types of dystrophies or healthy individuals[22]. Another study showed that wheelchair users have a higher percentage of MG than ambulant patients[23].

Only two studies analyzed the PA of individuals with DMD, and the data showed that individuals with DMD had low PA values compared to the reference values[6,8].

None of the studies demonstrated a correlation between PA and other body composition variables, and only one study showed evidence of a correlation between PA and functional measures. According to the authors, individuals with the highest PA had the shortest time to complete the ten-meter walk test and the highest total MFM score[6].

DISCUSSION

Body composition analysis is an important component of the assessment of individuals with DMD. By analyzing body composition, it is possible to estimate the results of therapies that aim to preserve muscle mass when analyzing fat-free mass. On the other hand, an increase in fat mass can be correlated with the progression of the disease which, in its clinical course, evolves with muscle degeneration and its replacement by connective and fatty tissue[24].

There are various methods for assessing body composition, and the main ones identified in this study were: BIA, dual-energy X-ray absorptiometry (DXA), labeled water dilution (WD) and skinfold measurements (ST) 7,19,21. The WD and DXA methods are considered accurate and precise for assessing response to therapy or longitudinal monitoring, but they are expensive and require technological equipment[7,19]. Alternatively, BIA is a valid and more accessible method from a clinical and financial perspective for estimating the percentage of fat-free mass (FFM) in healthy populations and populations with specific diseases[21].

The maintenance of FFM in patients with DMD is an important factor, as it is related to muscle function and quality of life[21,25]. In their study, Grilo et al. (2020) observed a high percentage of FM (30.1 ± 18.5) in individuals with DMD compared to the reference values proposed by other authors[21]. Similarly, other studies have also observed an excessive percentage of FM in patients with DMD, where values of 19.8 to 41.4% of FM were found in different age groups[7,19].

Jacques et al. (2018) analyzed physical activity by accelerometry and the percentages of FFM and FM of individuals with different types of dystrophies and controls. The authors reported that the groups of patients with muscular dystrophies had 34-46% more FM than the control group. In this same study, the group with DMD had 21-28% less FFM than all the other groups, and it was also observed that the sedentary behavior of individuals with DMD was associated with the percentage of FFM. For Barja et al. (2016), the loss of FFM and the increase in FM in children with neuromuscular diseases can aggravate the progression of the disease. According to the authors, obesity leads to increased respiratory work, overloading previously weakened respiratory muscles, concomitantly accentuating immobility and loss of bone mass, which impair the rehabilitation process[23]. Malnutrition, on the other hand, tends to aggravate the progression of the disease, favoring respiratory infections that affect lung function[26].

Specifically, in patients with DMD, the percentage of FM also seems to be related to functional worsening. Individuals with DMD tend to show progressive muscle weakness in the lower limbs, progressing from proximal to distal extremities, which leads to functional repercussions such as abnormal gait, frequent falls and difficulty climbing stairs, progressing to loss of gait[24]. According to Saure et al. (2018), the percentage of MG was significantly higher in individuals with DMD who lost their gait than in those whose gait was preserved (72% vs. 46%, $p < 0.05$). In addition to FM and FFM, another important body composition variable is PA 8,25. According to Vermeulen et al. (2019), boys with DMD have lower PA values than their healthy peers. In their study, the authors observed that individuals with DMD aged between 2 and 9 had PA values lower than 3.0°. In healthy children aged between 5 and 9 years, the PA values varied between 4° and 4.3° [27].

In different types of diseases, the analysis of PA has prognostic value in relation to the progression of the disease, the incidence of post-operative complications, the length of hospital stays and mortality[9]. In DMD, patients with a higher functional score and better performance in functional tests had a greater phase angle[6]. As DMD progresses, cell degeneration is accentuated and, consequently, there is greater functional decline and a lower phase angle[6]. These findings may suggest that PA also has important prognostic value in DMD[6].

Thus, the data presented by the studies show that the loss of cell membrane integrity and the consequent degeneration of muscle fibers can influence the body composition of these individuals, with a higher percentage of FM and a lower percentage of FFM, when compared to healthy individuals[22]. In this same morbidity, the absence of the dystrophin protein results in instability in muscle cell membranes, which is related to a decrease in PA[8].

In more advanced stages of DMD, PA values continue to be lower than those observed in healthy individuals, the percentage of MG is significantly higher, and PA values and functional performance are lower[6,23].

Considering that PA is influenced by age [27], the main limitation of this review refers to the sample of studies included, which includedpatients from different age groups.

Finally, although PA has a prognostic value in DMD, further studies should be conducted to confirm these findings at different stages of the disease's development, as well as correlate them with measures of motor function and muscle strength. It is possible that, with these results, therapies aimed at preserving muscle mass and reducing the increase in adipose tissue can be controlled by their respective health professionals.

CONCLUSION

The set of scientific articles used in this narrative review indicated that the changes in the percentages of FFM and FM observed in DMD are related to PA values. All three variables change as the disease progresses. However, it is not yet clear whether and how these changes are related to one another as they progress. Therefore, the prognostic and therapeutic potential of using PA in DMD needs to be scientifically explored through new studies and correlated with measures of functional performance and muscle strength.

REFERENCES

1. Annexstad EJ, Fagerheim T, Holm I, Rasmussen M. Molecular and Clinical Characteristics of a National Cohort of Paediatric Duchenne Muscular Dystrophy Patients in Norway. J Neuromuscul Dis 2019; 6: 349–59. DOI: 10.3233/JND-190402

2. Jaka O, Casas-Fraile L, López De Munain A, Sáenz A. Costamere proteins and their involvement in myopathic processes. Expert Rev Mol Med 2015; 17. DOI:10.1017/erm.2015.9.

3. Waldrop MA, Flanigan KM. Update in Duchenne and Becker muscular dystrophy. Curr Opin Neurol 2019; 32: 722–7. DOI: 10.1097/WCO.0000000000000739.

4. Leon MADS, Roza DL Da, Davoli GBDQ, Baptista CRDJA De, Sobreira CFDR, Mattiello-Sverzut AC. Generation of percentile curves for strength and functional abilities for boys with Duchenne muscular dystrophy. Muscle and Nerve 2023; 68: 198–205. DOI: 10.1002/mus.27921.

5. Billich N, Adams J, Carroll K, et al. The Relationship between Obesity and Clinical Outcomes in Young People with Duchenne Muscular Dystrophy. Nutrients 2022; 14: 1–15. DOI: 10.3390/nu14163304

6. Souza MA de, Cezarani A, Lizzi EA da S, et al. The use of the gait profile score and gait variable score in individuals with Duchenne Muscular Dystrophy. J Biomech 2020; 98. DOI:10.1016/j.jbiomech.2019.109485.

7. Mok E, Letellier G, Cuisset J-M, Denjean A, Gottrand F, Hankard R. Assessing change in body composition in children with Duchenne muscular dystrophy: anthropometry and bioelectrical impedance analysis versus dual-energy X-ray absorptiometry. Clin Nutr 2010; 29: 633–8. DOI: 10.1016/j.clnu.2010.03.011.

8. Vermeulen KM, Lopes MMGD, Grilo EC, et al. Bioelectrical impedance vector analysis and phase angle in boys with duchenne muscular dystrophy. Food Nutr Res 2019; 63: 1–9. DOI: 10.29219/fnr.v63.1615.

9. Martins PC, Alves Junior CAS, Silva AM, Silva DAS. Phase angle and body composition: A scoping review. Clin Nutr ESPEN 2023; 56: 237–50. DOI: 0.1016/j.clnesp.2023.05.015.

10. Gulin J, Ipavic E, Mastnak DM, Brecelj E, Edhemovic I, Kozjek NR. Phase angle as a prognostic indicator of surgical outcomes in patients with gastrointestinal cancer. Radiol Oncol 2023; 57: 524–9. DOI: 10.2478/raon-2023-0060.

11. Yoshimura Y, Wakabayashi H, Nagano F, et al. Phase angle is associated with sarcopenic obesity in post-stroke patients. Clin Nutr 2023; 42: 2051–7. DOI: 10.1016/j.clnu.2023.08.018.

12. Yokomachi J, Fukuda T, Mizushima Y, et al. Clinical usefulness of phase angle as an indicator of muscle wasting and malnutrition in inpatients with cardiovascular diseases. Asia Pac J Clin Nutr 2023; 32: 297–307. DOI: 10.6133/apjcn.202309_32(3).0001.

13. Kang SH, Do JY. Phase Angle as a Risk Factor for Mortality in Patients Undergoing Peritoneal Dialysis. Nutrients 2023; 15. DOI:10.3390/nu15234991.

14. Rosas-Carrasco O, Núñez-Fritsche G, López-Teros MT, et al. Low muscle strength and low phase angle predicts greater risk to mortality than severity scales (APACHE, SOFA, and CURB-65) in adults hospitalized for SARS-CoV-2 pneumonia. Front Nutr 2022; 9: 4–11. DOI: 10.3389/fnut.2022.965356.

15. Desport JC, Marin B, Funalot B, Preux PM, Couratier P. Phase angle is a prognostic factor for survival in amyotrophic lateral sclerosis. Amyotroph Lateral Scler 2008; 9: 273–8. DOI:10.1080/17482960801925039.

16. Radić M, Kolak E, Đogaš H, et al. Body composition parameters in systemic sclerosis—a systematic review and meta-analysis. Rheumatology 2024; 63: 16–25. DOI: 10.1093/rheumatology/kead418.

17. Pineda-Juárez JA, Lozada-Mellado M, Ogata-Medel M, et al. Body composition evaluated by body mass index and bioelectrical impedance vector analysis in women with rheumatoid arthritis. Nutrition 2018; 53: 49–53. DOI: 10.1016/j.nut.2018.01.004.

18. Norman K, Stobäus N, Pirlich M, Bosy-Westphal A. Bioelectrical phase angle and impedance vector analysis - Clinical relevance and applicability of impedance parameters. Clin Nutr 2012; 31: 854–61. DOI:10.1016/j.clnu.2012.05.008.

19. Mok E, Béghin L, Gachon P, Daubrosse C, Fontan J, Cuisset J. Estimating body composition in children with Duchenne muscular dystrophy: comparison of bioelectrical impedance analysis and. Am J Clin Nutr 2006; 83: 65–9.DOI:10.1093/ajcn/83.1.65.

20. Barja S, Pérez R. Clinical assessment underestimates fat mass and overestimates resting energy expenditure in children with neuromuscular diseases. Clin Nutr ESPEN 2016; 15: 11–5.DOI:10.1016/j.clnesp.2016.03.079.

21. Grilo EC, Cunha TA, Costa ÁDS, et al. Validity of bioelectrical impedance to estimate fat-free mass in boys with Duchenne muscular dystrophy. PLoS One 2020; 15: 1–12.DOI: 10.1371/journal.pone.0241722.

22. Jacques MF, Onambele-Pearson GL, Reeves ND, Stebbings GK, Smith J, Morse CI. Relationships between muscle size, strength, and physical activity in adults with muscular dystrophy. J Cachexia Sarcopenia Muscle 2018; 9: 1042–52.DOI:10.1002/jcsm.12347.

23. Saure C, Caminiti C, Weglinski J, de Castro Perez F, Monges S. Energy expenditure, body composition, and prevalence of metabolic disorders in patients with Duchenne muscular dystrophy. Diabetes Metab Syndr Clin Res Rev 2018; 12: 81–5.DOI:https://doi.org/10.1016/j.dsx.2017.08.006.

24. Maciel Pizzato T, Jesus Alves de Baptista CR de, Martinez EZ, Sobreira CF da R, Mattiello-Sverzut AC. Prediction of Loss of Gait in Duchenne Muscular Dystrophy Using the Ten Meter Walking Test Rates. J Genet Syndr Gene Ther 2016; 7: 1–6.DOI:10.4172/2157-7412.1000306.

25. Davis J, Samuels E, Mullins L. Nutrition Considerations in Duchenne Muscular Dystrophy. Nutr Clin Pract 2015; 30: 511–21.DOI:https://doi.org/10.1177/0884533615586202.

26. Pane M, Vasta I, Messina S, et al. Feeding problems and weight gain in Duchenne muscular dystrophy. Eur J Paediatr Neurol 2006; 10: 231–6.DOI:10.1016/j.ejpn.2006.08.008.

27. Mattiello R, Mundstock E, Ziegelmann PK. Brazilian Reference Percentiles for Bioimpedance Phase Angle of Healthy Individuals. 2022; 9: 1–7.DOI:10.3389/fnut.2022.912840.

28. Souza MA, Ferreira ME, de Baptista CRJA, Mattiello-Sverzut AC. Gasto energético na marcha de crianças com distrofia muscular de Duchenne: estudo de caso. Fisioter Pesq. 2014;21(2):193-198. DOI: 10.1590/1809-2950/63621022014