Can magnesium supplementation boost neuromuscular adaptations when combined with resistance training in Long COVID patients?

Gabriel Carvalho Rocha, Markus Filardi Moura Olinto, Victor César Dias Lins , Marco Aurélio Araújo Dourado , Maurílio Tiradentes Dutra

https://doi.org/10.1590/SciELOPreprints.12255

Submetido em: 2025-06-16
Postado em: 2025-06-16 (versão 1)
(AAAA-MM-DD)

Can magnesium supplementation boost neuromuscular adaptations when combined with resistance training in Long COVID patients?

Gabriel Carvalho Rocha

Faculdade de Educação Física, Universidade de Brasília, Brasília, DF, Brasil. ORCID: https://orcid.org/0009-0009-9726-8911

Markus Filardi Moura Olinto

Faculdade de Educação Física, Universidade de Brasília, Brasília, DF, Brasil. ORCID: https://orcid.org/0009-0002-1242-812X

Victor César Dias Lins

Faculdade de Educação Física, Instituto Federal de Brasília, Brasília, DF, Brasil. ORCID: https://orcid.org/0009-0006-5621-3787

Marco Aurélio Araújo Dourado

Faculdade de Educação Física, Instituto Federal de Brasília, Brasília, DF, Brasil. ORCID: https://orcid.org/0009-0004-9348-6384

Maurílio Tiradentes Dutra

Faculdade de Educação Física, Instituto Federal de Brasília and Universidade de Brasília, Brasília, DF, Brasil. ORCID: https://orcid.org/0000-0001-6245-3337

ABSTRACT

Background: The novel coronavirus triggered a global pandemic in March 2020, leading to millions of fatalities worldwide. Some individuals suffer from symptoms that persist after the infection ends and this has been named Long COVID. Fatigue and muscle weakness are among the most prevalent Long COVID symptoms. Resistance training (RT) and magnesium supplementation may be feasible strategies to induce neuromuscular adaptations and rehabilitate Long COVID patients' strength. Aim: to investigate the effect of RT and magnesium supplementation on muscle mass, strength, and functional capacity in Long COVID patients. **Methods:** Eight women (43.1 ± 16.3 years; 27.8 ± 8.9 kg/m^2) completed a 6-weeks traditional RT (TRAD, n=4) protocol or a 6-weeks RT protocol combined with magnesium dimalate (400mg/d) supplementation (SUP, n=4). Long COVID symptoms score, handgrip strength, biceps *brachialis* thickness, and functional performance (*timed up and go*; *five times sit to stand test*) were assessed before and after the intervention. Repeated measures

ANOVA was used to analyze within-between groups interaction. **Results:** The symptom score was significantly reduced after the intervention only in the SUP group (1996.9 ± 425.2 AU *vs* 1309.4 ± 416.4 AU, $p < .05$). Handgrip strength slightly increased in both groups without reaching statistical significance (+3.6% and +9.4% in TRAD and SUP, respectively, $p > .05$). Time spent performing the five times sit to stand test slightly decreased in both groups without reaching statistical significance (-3.7% and -3.4% in TRAD and SUP, respectively, $p > .05$). The timed up and go performance slightly improved only in the TRAD group (-9.4%, $p > .05$), whereas biceps thickness slightly increased only in the SUP group (+13.6%, $p > .05$). **Conclusion:** magnesium dimalate supplementation cannot significantly boost neuromuscular adaptations compared to RT alone. However, it can significantly reduce Long COVID symptoms score after 6 weeks of intervention.

Keywords: Strength training, Magnesium Dimalate, Supplementation, Persistent Covid-19.

Introduction

The novel coronavirus, responsible for severe acute respiratory syndrome (SARS-CoV-2, known as COVID-19), triggered a global pandemic in March 2020, leading to millions of fatalities worldwide [1]. The skeletal muscle tissue may be negatively affected by COVID-19. Fiber necrosis mediated by inflammation and motoneuron degeneration are possible mechanisms of skeletal muscle damage after the coronavirus invades it [2]. This damage may lead to medium- and long-term muscle weakness, exercise intolerance, and fatigue.

Thus, some individuals suffer from symptoms that persist after the infection ends [3]. This has been referred to as Long Covid. According to Ely and colleagues (2024), Long COVID is a chronic condition associated with infection after SARS-CoV-2 infection that has symptoms present for at least 3 months continuously [4]. The number of people with Long COVID now would be approximately between 248 and 380 million worldwide. Prolonged muscle weakness and fatigue are amongst the most-reported persistent symptoms affecting approximately 45% of individuals with Long Covid [5].

Skeletal muscle plays a critical role in several physiological processes, including glucose regulation and protein synthesis [6]. Hence, muscle mass gain and strengthening strategies in Long COVID are critical for optimizing rehabilitation.

Resistance training (RT) is a promising approach as it is highly effective for promoting muscle strength and hypertrophy [7] . Furthermore, magnesium supplementation has emerged as a potential alternative strategy to rehabilitate Long Covid patients due to its metabolic functions, such as muscle contraction, protein synthesis, and energetic and nerve impulse regulation [8] .

Also, it is argued that magnesium supplementation could ameliorate some of the Long Covid-like symptoms, reduce the severity of the symptoms and facilitate recovery [9] . Magnesium dimalate, a combined form of magnesium and malic acid, has high bioavailability and is easy absorbed [10] . Therefore, the combination of RT with magnesium dimalate supplementation could be a potent Long Covid rehabilitation strategy. However, this hypothesis has yet to be tested. The aim of this study was to investigate the effect of RT combined with magnesium dimalate supplementation on muscle mass, strength, and functional performance.

Methods

Study design and sample

This study included women over 18 years old, physically inactive for the last six months, non-smokers, and exhibiting symptoms that could be associated with Long COVID for at least three months after the end of the acute infection. The intervention lasted six weeks. Dependent variables were measured before and after. Eight participants signed the Informed Consent Form and finished the procedures. The study followed the Helsinki Declaration and was approved by the institution's Research Ethics Committee under the protocol number: 6.313.134.

The sample was divided into two groups. The first group performed a traditional RT protocol (TRAD, n = 4) and the second group performed the same RT protocol with magnesium dimalate supplementation (SUP, n = 4). Allocation of the first participant was randomized by sortition. Then, allocation followed the order of entrance into the study.

Resistance training protocol

The training protocol consisted of seven upper and lower limb exercises. The order was: 1) trunk flexion on the ground; 2) bench press machine; 3) pull-up machine; 4) extension chair; 5) elbow extension with dumbbell; 6) elbow flexion with dumbbell; 7) knee flexor chair. The volunteers performed 2 sets of 10 to 12 repetitions, with intensity between 5 and 6 in the OMINI-RES subjective exertion scale. The rest interval between sets and exercises was between one and two minutes. The oxygen saturation of all participants was monitored during the training sessions, and “desaturation” was a drop of 3-4% of baseline saturation or less than 94%, which would result in the end of the training session for the participant, as recommended by DeMars et al. (2022) [11]. No participant in this study had their session terminated early due to desaturation.

Magnesium Supplementation

At the beginning of the intervention, participants received bottles containing 400mg capsules of commercially available magnesium dimalate (Naiak®). Daily dosage was 400mg. Volunteers were instructed to take one capsule per day throughout the intervention period, preferably after lunch, and not to use other dietary supplements during the intervention. At the end of the intervention, they returned the bottles for counting the remaining capsules. Adherence to supplementation was at least 80% as per the remaining capsules count.

Long Covid Symptoms

The severity and prevalence of Long Covid symptoms were assessed using the DePaul Symptom Questionnaire – COVID (DSQ-COVID) translated to Portuguese and converted into a digital format. The questionnaire results were calculated according to the method recommended by the DSQ-COVID researchers [12] resulting in a score between 0 and 100 for each symptom. To obtain a single value that could represent all symptoms collectively, the scores of each symptom were summed. This summed score was used to perform the comparisons.

Muscle Thickness, Strength, and Functional Performance

Body mass was assessed using a digital scale (OMRON HBF-510, OMRON Healthcare Inc. Lake Forest, IL). Height was measured using a portable ultrasonic stadiometer (Inlab®), and the body mass index (BMI) was calculated by dividing body mass by height squared (kg/m²). Brachial biceps muscle thickness was assessed by a trained technician using a portable A-type (2,5Mhz) ultrasound device (Body Metrix 200). The measurement was performed in the dominant arm following all manufacturer recommendations [13].

Handgrip strength (HGS) assessment was performed with a hydraulic hand dynamometer (SAEHAN®) following literature recommendation [14]. Each participant performed three sets of 3 seconds of maximum isometric contraction in the dominant hand, with a 30-second interval between sets. The highest value obtained was used for analysis. The Five Times Sit-to-Stand Test (5TSTS), Timed Up and Go (TUG), and Six-Minute Walk Test (6MWT) were assessed as measures of functional performance. The test procedures followed the protocols and guidelines previously described [15,16].

Statistical Analysis

The Jamovi statistical package (version 2.3.28) was used for statistical analysis, adopting a significance level of $P < 0.05$. Shapiro-Wilk tested the data distribution. T-test compared descriptive characteristics before the intervention. Then, a repeated measures analysis of variance within-between groups (ANOVA, 2 groups * 2 moments) was performed. Tukey's post hoc analysis was used to identify possible differences.

Results

Table 1 presents the descriptive characteristics of the sample divided by group. No statistical significance was observed when comparing the groups. The supplementation group presented a BMI classification of obesity, while traditional group was eutrophic.

Table 1. Descriptive characteristics of the sample before the intervention.

Variable	Trad (n=4)	Sup (n=4)
Age (years)	47.3 ± 19.8	39.0 ± 13.4
Height (cm)*	162.1 (161.6 – 163.8)	159.3 (158.5 – 161.4)
Body mass (kg)	64.1 ± 8.8	86.8 ± 29.9
BMI (kg/m^2)	24.1 ± 3.9	31.5 ± 11.6

Notes: *Violated the normality test, data is presented as median (25th – 75th percentile).

Table 2 presents dependent variables from both groups before and after the intervention. No statistical significance was observed within or between groups in muscle strength, thickness, and functional performance ($p > .05$). Slight improvements were observed. Handgrip strength increased in both groups (+3.6% and +9.4% in TRAD and SUP, respectively, $p > .05$). Time spent performing the five times sit to stand test decreased in both groups (-3.7% and -3.4% in TRAD and SUP, respectively, $p > .05$). The timed up and go performance slightly improved only in the TRAD group

(-9.4%, p > .05), whereas biceps thickness increased only in the SUP group (+13.6%, p > .05).

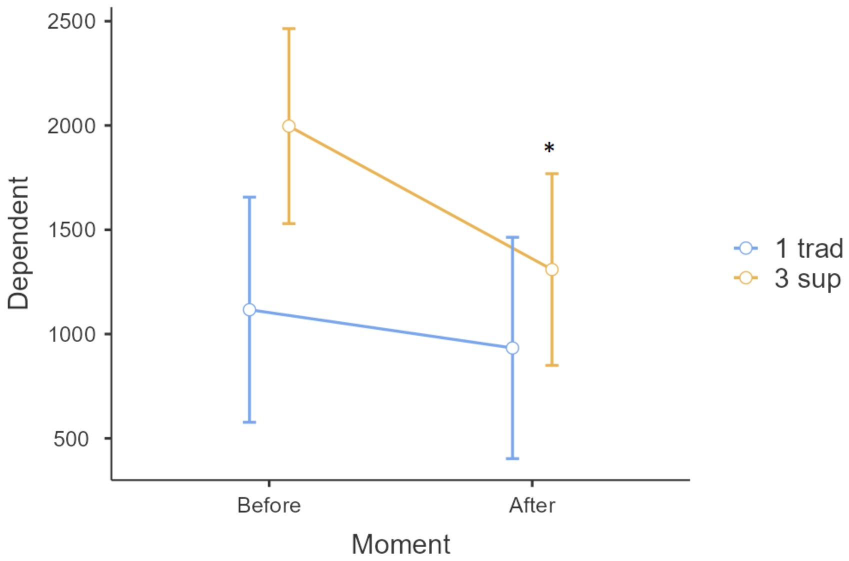
Table 2. Characteristics of the sample before and after the intervention.

	Before		**After**	
Variable	**Trad**	**Sup**	**Trad**	**Sup**
HGS (kg/f)	28.5 ± 5.7	31.8 ± 9.5	29.5 ± 7.0	34.0 ± 8.0
5TSTS (s)	10.8 ± 2.2	10.6 ± 1.7	10.3 ± 1.1	10.1 ± 2.0
TUG (s)	8.7 ± 2.7	8.3 ± 2.3	7.7 ± 1.6	8.6 ± 2.5
Muscle thickness (mm)	23.8 ± 2.1	19.2 ± 3.9	23.2 ± 0.7	21.2 ± 2.2

Note: The results are presented as Mean ± Standard Deviation. No statistical significance was observed. HGS: handgrip strength. 5TSTS: five times sit to stand test. TUG: timed up and go.

Figure 1 presents the result of the Long Covid symptom score (DSQ-Covid). There was a significant time effect ($F = 15.95$, $p = 0.01$, partial $eta^2 = 0.76$). Only the supplementation group showed a significant reduction after the intervention, although with no difference compared to RT without supplementation.

Figure 1. DSQ-Covid score before and after the intervention.



Note: * P = 0.018 compared to before (within group).

Discussion

The aim of the present study was to investigate the effect of RT on muscle thickness, strength, functional performance and overall symptoms severity in Long Covid patients. The main result was that no significant differences between groups were observed. Within groups, only the supplementation showed a significant reduction in the symptoms score after the intervention. No other differences were observed in any other variable.

The absence of differences within and between groups indicates that RT with and without magnesium supplementation evoke similar and only slightly effects on muscle thickness, strength, and performance in the context of Long COVID rehabilitation after six weeks. Of note, this is a short period of intervention with a training frequency of only two times a week, and a moderate to prevent post-exertional malaise (PEM), a worsening of symptoms that may happen in Long COVID patients following physical activity [17] .

In this sense, protocol characteristics may be responsible for the absence of statistical significance. For instance, muscle hypertrophy tends to occur after more prolonged RT programs (12 weeks on) [18] . Moreover, Ramírez-Vélez et al. [19] showed no significant increase in grip strength after 6 weeks of progressive RT in Long Covid patients. Still, they found significant increases in dynamic 1RM (repetition maximum) tests, such as pectoral, leg press, knee extension, and trunk press. We did not run these tests in the present study.

However, Ibrahim et al. [20] assessed handgrip strength in a sample that performed RT exercises with sandbags, dumbbells, and elastic bands. They found a remarkable 130% improvement in handgrip strength after 6 weeks. Sample characteristics may account for the greater magnitude of strength improvement in that study as their sample was composed of sarcopenic, chronic kidney diseased individuals with Long COVID, that is, a more fragile sample at the beginning of the intervention compared to the present study, that is, with a higher potential to improve.

The reduction of the symptoms score reached statistical significance only in the supplementation group. At first sight, this indicate that magnesium dimalate may contribute to Long Covid rehabilitation in the short term, as it could be hypothesised based on recent literature and metabolic functions of magnesium [8,9] . However, percent changes from pre-to-post intervention were very similar in both groups (37.5% and 34.5% in TRAD and SUP, respectively). So, this significance may be related to the higher initial value of the score in the SUP group, even though not statistically different from TRAD.

In this sense, the small sample size is a limitation of this report and may reflect type II errors in the comparisons due to a lack of statistical power. The lack of a control group with supplementation without training is also a limitation. So, it is difficult to affirm that magnesium supplementation adds a significant effect to RT during Long Covid rehabilitation in the first six weeks of training. However, it is worth mentioning that even with a low frequency, moderate intensity protocol, a tendency to improve strength and performance was observed, together with a clinically relevant reduction in the severity of the symptoms in both groups (around 35%).

Despite the limitations regarding sample size, control group and protocol characteristics, this report is the first study no asses the combination of RT and magnesium supplementation in a sample of Long Covid Brazilian women (to the best of our knowledge). RT is well known to induce strength gain and optimize health parameters in a wide range of clinical populations [7], and the ±35% symptoms score reduction in the present study has the potential to improve quality of life.

In summary, RT for six weeks is safe, leads to slight improvements in neuromuscular variables and clinically relevant reduction in long covid symptomatology. Magnesium supplementation is also safe, as no side effects of the supplementation was reported, but does not significantly add additional benefits to RT after 6 weeks. Future studies should analyse larger samples, more intense RT protocols and a longer magnesium supplementation duration.

Acknowledgements

This work was supported by the Research Support Foundation of the Federal District, Brasilia, Brazil (FAPDF).

References

1. World Health Organization. WHO COVID-19 dashboard. https://data.who.int/dashboards/covid19/deaths?n=o (2025).
2. Soares, M. N. *et al.* Skeletal muscle alterations in patients with acute Covid-19 and post-acute sequelae of Covid-19. *Journal of Cachexia, Sarcopenia and Muscle* vol. 13 11–22 Preprint at https://doi.org/10.1002/jcsm.12896 (2022).
3. Bigdelou, B. *et al.* COVID-19 and Preexisting Comorbidities: Risks, Synergies, and Clinical Outcomes. *Front Immunol* **13**, (2022).

4. Ely, E. W., Brown, L. M. & Fineberg, H. V. Long Covid Defined. *New England Journal of Medicine* **18**, 1746–1753 (2024).

5. Salari, N. *et al.* Global prevalence of chronic fatigue syndrome among long COVID-19 patients: A systematic review and meta-analysis. *Biopsychosoc Med* **16**, (2022).

6. Gil, S. *et al.* Muscle strength and muscle mass as predictors of hospital length of stay in patients with moderate to severe COVID-19: a prospective observational study. *J Cachexia Sarcopenia Muscle* **12**, 1871–1878 (2021).

7. Lopez, P. *et al.* Resistance Training Load Effects on Muscle Hypertrophy and Strength Gain: Systematic Review and Network Meta-analysis. *Medicine and Science in Sports and Exercise* vol. 53 1206–1216 Preprint at https://doi.org/10.1249/MSS.0000000000002585 (2021).

8. Gröber, U., Schmidt, J. & Kisters, K. Magnesium in prevention and therapy. *Nutrients* vol. 7 Preprint at https://doi.org/10.3390/nu7095388 (2015).

9. Trapani, V. *et al.* The relevance of magnesium homeostasis in COVID-19. *European Journal of Nutrition* vol. 61 Preprint at https://doi.org/10.1007/s00394-021-02704-y (2022).

10. Ogawa, L. S. Revisão narrativa da biodisponibilidade e dos efeitos de diferentes formulações de sais de magnésio. (Universidade Federal de Ouro Preto, Ouro Preto, MG, Brasil, 2022).

11. DeMars, J. *et al.* What is Safe Long COVID Rehabilitation? *Journal of Occupational Rehabilitation* vol. 33 Preprint at https://doi.org/10.1007/s10926-022-10075-2 (2023).

12. Jason, L. A. & Dorri, J. A. ME/CFS and Post-Exertional Malaise among Patients with Long COVID. *Neurol Int* **15**, (2023).

13. Abe, T., DeHoyos, D. V., Pollock, M. L. & Garzarella, L. Time course for strength and muscle thickness changes following upper and lower body resistance training in men and women. *Eur J Appl Physiol Occup Physiol* **81**, (2000).

14. Reis, M. M. & Arantes, P. M. M. Medida da força de preensão manual – validade e confiabilidade do dinamômetro saehan. *Fisioterapia e Pesquisa* **18**, 176–181 (2011).

15. Centers for Disease Control and Prevention. Timed Up & Go (TUG). https://www.cdc.gov/steadi/media/pdfs/steadi-assessment-tug-508.pdf (2017).

16. De Melo, T. A. *et al.* The five times sit-to-stand test: Safety and reliability with older intensive care unit patients at discharge. *Rev Bras Ter Intensiva* **31**, (2019).

17. Gloeckl, R. *et al.* Practical Recommendations for Exercise Training in Patients with Long COVID with or without Post-exertional Malaise: A Best Practice Proposal. *Sports Med Open* **10**, (2024).

18. Kaczmarczyk, K., Płoszczyca, K., Jaskulski, K. & Czuba, M. Eight Weeks of Resistance Training Is Not a Sufficient Stimulus to Improve Body Composition in Post-COVID-19 Elderly Adults. *J Clin Med* **14**, (2025).

19. Ramírez-Vélez, R. *et al.* Exercise training in long COVID: the EXER-COVID trial. *Eur Heart J* (2024) doi:10.1093/eurheartj/ehae721.

20. Ibrahim, A. A. *et al.* Influences of high vs. low-intensity exercises on muscle strength, function, and quality of life in post-COVID-19 patients with sarcopenia: a randomized controlled trial. *Eur Rev Med Pharmacol Sci* 9530–9539 (2023).

Authors' contribution

Gabriel Carvalho Rocha: conceptualization, data curation, formal analysis, investigation, methodology, writing – original draft.

Markus Filardi Olinto: conceptualization, data curation, formal analysis, investigation, methodology, writing – original draft.

Victor César Dias Lins: conceptualization, data curation, formal analysis, investigation, methodology.

Marco Aurélio Araujo Dourado: conceptualization, data curation, investigation, methodology.

Maurílio Tiradentes Dutra: conceptualization, data curation, funding acquisition formal analysis, supervision, software investigation, methodology, writing – original draft.

Declaration of conflict of interest

The authors declare that there is no conflict of interest.

Declaration of availability of research data

The data set supporting the results of this study is not publicly available.