

Covid-19 symptom severity is associated with visceral fat and total testosterone in men



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Abstract The testicles are potential targets of SARS-CoV-2, making them susceptible to oxidative stress and tissue damage. The effects of SARS-CoV-2 infection on testosterone secretion, muscle mass, and strength remain unclear. This study aimed to analyze body fat, muscle mass, strength, and testosterone in men with and without a history of COVID-19, and to investigate the association between symptom severity and testosterone, muscle mass, strength, and body fat. This cross-sectional study included 46 men (median age: 24.5 years; BMI: 24.9 kg/m²) with and without a history of COVID-19 and recovered for at least 12 months. For comparison purposes, participants were grouped as follows: 1) No COVID-19 diagnosis *versus* positive COVID-19 diagnosis; 2) no or mild symptoms *versus* moderate or severe symptoms. Participants with a COVID-19 positive diagnosis were older (26.0 {23.8 – 37.3} vs. 21.0 {19.0 – 22.8} years, $P = 0.003$) and presented less free testosterone (9.0 ± 5.5 vs. 16.3 ± 10.5 ng/dL, $P = 0.03$) compared to the nondiagnosed ones. Also, they presented lower levels of relative handgrip strength (11.1% lower, medium effect size) and total testosterone (26.0% lower, medium effect size). Participants who experienced moderate or severe symptoms presented higher age, weight, BMI, fat mass, visceral fat, and absolute handgrip strength, with effect sizes ranging from medium to large. Also, they presented a 32.3% lower total testosterone level, as well as a 33.0% higher body fat compared to mild symptoms. In conclusion, COVID-19 symptom severity is linked to more visceral fat and lower testosterone levels after recovery but does not significantly impact muscle mass or strength in men after 12 months. This finding is of critical importance for male reproductive health.

Keywords: body fat, muscle mass, muscle strength, sars-cov-2

1. Introduction

The novel coronavirus, which is 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. The initial clinical manifestations of the disease include fever, severe inflammation of the respiratory tract, cough, dyspnea, fatigue, myalgia, and other symptoms. Elderly individuals and those with preexisting conditions, such as obesity and respiratory disorders, are more prone to developing severe acute respiratory infections and, in many cases, succumb to the disease (Oliveira, 2022).

Research has progressively revealed the characteristics of SARS-CoV-2, including its mechanisms of invasion and replication. The virus enters host cells via angiotensin-converting enzyme 2 (ACE2) receptors on the cell membrane (Almeida et al., 2021). Once inside the body, the virus has a strong affinity for respiratory system cells, triggering an exaggerated inflammatory response, interstitial inflammation, diffuse alveolar damage, and impaired gas exchange (Lima et al., 2021).

In addition to its primary impact on the respiratory system, SARS-CoV-2 can cause systemic endocrine and metabolic dysfunctions marked by heightened inflammation, affecting multiple organs (Bornstein et al., 2020). Postmortem studies have identified viral genetic material in the testes, revealing pathological changes such as a reduction in Leydig cell populations, which are responsible for testosterone production (Nie et al., 2021; Yang et al., 2020). This testicular vulnerability may stem from the high expression of ACE2 in testicular tissue (Fan et al., 2021).

As a result, the testes are considered a potential target for SARS-CoV-2, potentially experiencing oxidative stress at systemic levels. This raises concerns about the short-, medium-, and long-term effects of the virus on testosterone production, even among men with mild symptoms (Fustino et al., 2022). This study aims to explore the impact of SARS-CoV-2 on testosterone secretion and its subsequent effects on lean body mass (e.g., muscle mass) and strength, both of which are regulated by testosterone levels (Schoenfeld, 2010).



A review of the literature suggests that low testosterone levels exacerbate the severity of COVID-19 in elderly men (Papadopoulos et al., 2021). Additionally, the quantity and quality of lean mass are correlated with shorter hospital stays in COVID-19 patients with mild to moderate infections, indicating that patients with greater muscle strength and lean mass recover faster (Gil et al., 2021). On the other hand, COVID-19 has been associated with a significant decline in handgrip muscle strength, suggesting chronic muscle tissue damage caused by the disease (Del Brutto et al., 2021).

Excessive fat mass (e.g., obesity) and sedentary behavior are recognized as major risk factors for severe COVID-19 outcomes (Zeigler & Acevedo, 2024), both of which are associated with reductions in muscle mass and strength. Given the critical role of muscle tissue in physiological processes such as glucose regulation, the immune response, the basal metabolic rate, and protein synthesis (Gil et al., 2021), assessing testosterone levels, muscle mass, fat mass, and muscle strength is crucial in the context of COVID-19 prevention.

Notably, previous studies have reported that men diagnosed with COVID-19 exhibit lower testosterone levels than their healthy peers do for up to 80 days (Cannarella et al., 2024), three months (Enikeev et al., 2022), and even seven months postinfection (Salonia et al., 2023). However, the long-term consequences of reduced testosterone levels on skeletal muscle mass and strength remain unclear. Furthermore, the relationships between disease severity and changes in testosterone, body composition (e.g., muscle and fat mass), and strength have yet to be fully elucidated.

Therefore, this study aimed to investigate serum testosterone levels, body fat, muscle strength, and muscle mass in men with and without a COVID-19 diagnosis and to compare these variables according to symptom severity. It is hypothesized that a positive diagnosis is related to reduced muscle mass, strength, and testosterone levels and that greater symptom severity leads to more pronounced decreases in these outcomes.

2. Materials and methods

2.1. Study design and sample

This study adopted a cross-sectional design. The sample was recruited from health science students from two local institutions. Recruitment was conducted via Instagram groups and word-of-mouth in classroom settings. The inclusion criteria were male, aged between 18 and 43 years, and actively enrolled in undergraduate or postgraduate courses. The exclusion criteria were female sex, the use of anabolic steroids or testosterone replacement therapy, and the presence of health conditions that precluded participation in the tests.

The sample size was calculated via the online tool *Survey Monkey* (<https://pt.surveymonkey.com/mp/sample-size-calculator/>). With an estimated population of 2,000 students, a confidence level of 80% and a margin of error of 10% were used, resulting in the required sample size of 41 participants. Although 58 men volunteered, 12 failed to attend the scheduled testing sessions, resulting in a final sample of 46 participants (median age: 24.5 years, median BMI: 24.9 kg/m²). All people enrolled in the study completed an electronic questionnaire on health and lifestyle habits, including questions about their COVID-19 diagnosis and symptoms. The information gathered included comorbidities, current health status, dietary habits, use of supplements or medications, and COVID-19-related symptoms. This information was used to group participants on the basis of the following factors:

1. Diagnosis status: Presence vs. absence of a positive COVID-19 diagnosis.
2. Symptom severity: Absence or mild symptoms vs. moderate/severe symptoms.

These grouping factors were treated as independent variables, whereas hormonal, strength, and body composition measures were considered dependent variables.

Symptoms were characterized on the basis of the literature (Engstrom et al., 2020) as follows:

1. Mild symptoms included fever, fatigue, dry cough, nasal congestion, headache, conjunctivitis, sore throat, diarrhea, loss of taste or smell, and rash. Recovery occurred without hospitalization.
2. Moderate symptoms: Similar to mild symptoms, with additional dyspnea or decreases in oxygen saturation. Recovery occurred after hospitalization, without intubation.
3. Severe symptoms: Same as moderate symptoms, with further involvement of respiratory or other systems, exacerbation of preexisting conditions, or new complications requiring hospitalization and intubation.

2.2. Anthropometry and body composition

Body mass was measured via a digital scale (capacity 150 kg), and height was measured via a portable stadiometer. BMI was calculated as body mass divided by the square of height (kg/m²). Body composition was assessed via dual-energy X-ray absorptiometry (DEXA) via a GE Medical Systems Lunar 8743 model with Encore 2005 software. The participants removed metal objects to prevent interference and were placed in the supine position in the center of the DEXA table. The following variables were analyzed: total fat mass (kg), total fat percentage (%), and trunk fat mass (kg) as indicators of visceral fat and total lean mass (kg).

2.3. Muscle strength

Handgrip strength (HGS) was assessed via a SAEHAN™ hydraulic dynamometer. Each participant performed three maximum isometric contractions (5 seconds each) with a 30-second interval. The highest value among the sets was used as the absolute HGS. The device was individually adjusted, and the participants were seated according to the American Society of Hand Therapists' guidelines (Reis & Arantes, 2011). Relative muscle strength (RMS) was calculated by dividing HGS by BMI (HGS/BMI) to account for differences in body size and composition (Almeida et al., 2022).

2.4. Hormonal markers

Total and free testosterone blood concentrations were determined from arm blood samples and analyzed in an external laboratory via appropriate assays for each marker. Of the 46 participants, 24 consented to the blood test.

2.5. Statistical analysis

Data analysis was performed via Jamovi for Windows (version 2.3.28), with a significance level of $P \leq 0.05$. The Shapiro–Wilk test was used to assess the distributions of the dependent variables. The comparison of dependent variables across groups (e.g., presence vs. absence of diagnosis; mild vs. moderate/severe symptoms) was conducted via either Student's *t* test or the Mann–Whitney U test, depending on the data distribution. The effect sizes were interpreted as follows:

- Cohen's *d* for *t* tests (small: 0.2–0.5, moderate: 0.5–0.8, large: >0.8).
- Order biserial correlation for Mann–Whitney U tests (very small: 0.05–0.09, small: 0.1–0.19, medium: 0.2–0.29, large: 0.3–0.39, very large: ≥ 0.4).

3. Results

The descriptive characteristics of the sample according to group classification are shown in Table 1.

Table 1 Descriptive characteristics and comparisons according to group classification: with or without a positive diagnosis of COVID-19 and severity of symptoms.

	Diagnosis				Symptoms			
	Positive (n=36)	Negative (n=10)	<i>P</i>	ES	No/Mild (n=32)	Moderate/Severe (n=14)	<i>P</i>	ES
Age (years)	26.0 (23.8-37.3)	21.0 (19-22.3)	.00	.63 [#]	24.0 (22.0-33.0)	31.0 (24.3-39.8)	.11	.30 [#]
Weight (kg)	78.1 (71.2-87.3)	71.9 (63.7-86.1)	.46	.16	73.0 (68.1-86.2)	81.2 (77.4-93.0)	.24	.29 ^a
Height (cm)	178.0 ± 5.9	178.0 ± 6.7	.94	.02	177.5 ± 6.4	177.7 ± 5.3	.91	.03
BMI (kg/m ²)	25.1 (22.3-27.6)	23.1 (21.3-25.7)	.31	.21 ^a	23.7 (21.6-26.8)	25.4 (24.9-29.2)	.09	.32 [#]
Lean Mass (kg)	55.6 (51.0-60.9)	55.2 (52.6-56.3)	.67	.09	55.3 (51.9-57.0)	56.3 (51.8-60.4)	.65	.09
Fat Mass (kg)	18.0 (13.6-27.3)	13.7 (10.2-27.3)	.43	.17	15.2 (12.2-22.3)	22.7 (16.7-33.8)	.12	.29 ^a
Visceral Fat (kg)	9.9 (6.4-14.7)	7.0 (5.0-11.5)	.42	.17	7.6 (5.2-12.2)	12.5 (9.5-19.0)	.01	.31 [#]
Body Fat (%)	25.1 ± 9.8	24.1 ± 12.5	.80	.09	23.5 ± 9.7	28.1 ± 10.9	.17	.45 ^b
Absolute HGS (kgf)	40.7 ± 8.2	43.4 ± 8.9	.37	.32	40.6 ± 7.6	42.9 ± 9.8	.39	.28 ^a
Relative HGS (kgf/BMI)	1.6 (1.4-1.8)	1.8 (1.5-2.0)	.23	.25 ^a	1.6 (1.5-1.9)	1.6 (1.4-1.9)	.49	.13
TT* (ng/dL)	405.0 (329.0-554.0)	548.0 (408.0-614.5)	.29	.29 ^a	524.5 (351.0-582.0)	355.0 (300.5-407.3)	.07	.47 ^b
FT* (ng/dL)	9.0 ± 5.5	16.3 ± 10.5	.03	1.0 [#]	10.7 (7.2-14.2)	10.1 (6.9-12.6)	.79	.08

Notes: Values are presented as the means and standard deviations (Student's independent *t* tests) or medians and 25th and 75th percentiles (Mann–Whitney U tests). **n* = 24 (17 positive and 7 negative for COVID-19; 16 mild and 8 moderate symptoms). # Larger effect size. ^a Medium effect size. ^b larger effect size. Abbreviations: BMI: body mass index. HGS: handgrip strength. TT: total testosterone. FT: free testosterone.

The volunteers with a positive diagnosis were significantly older than those without the disease and presented significantly less free testosterone (34.8% lower). Although not statistically significant, there were indications of probable clinical relevance for other variables because of size and percentage variations. For example, individuals who tested positive for SARS-CoV-2 presented lower levels of relative handgrip strength (11.1% lower, medium effect size) and total testosterone (26.0% lower, medium effect size) and a higher BMI (8.7% higher) than those who had not contracted the virus.

A comparison of volunteers categorized into "no diagnosis or mild symptoms" and "moderate/severe symptoms" revealed clinically relevant trends despite the absence of statistical significance. Variables such as age, weight, BMI, fat mass, visceral fat, body fat percentage, visceral fat, absolute handgrip strength, and total testosterone exhibited meaningful differences. All of them, except total testosterone, were higher in the moderate/severe symptoms group, with effect sizes ranging from medium to large. Notably, patients who experienced moderate or severe COVID-19 had the lowest total testosterone levels (32.3% lower, large effect size, $P = 0.07$; Figure 1), even 12 months postdiagnosis, alongside increased body fat (+33%), weight (+10%), and BMI (+6.7%) (Table 1 and Figure 1). With respect to BMI, men with no/mild symptoms were eutrophic, whereas men with moderate/severe symptoms were overweight.

Notably, most of the individuals with a positive diagnosis were below the median for total and free testosterone (58.8%), as well as absolute and relative HGS (61.1%). Moreover, 87.5% of the participants who had moderate/severe COVID-19 symptoms were below the median testosterone level, whereas 68.8% of those who had no/mild symptoms were above the

median. In terms of visceral fat, 78.6% of the participants with moderate/severe symptoms were above the median (high fat), whereas 59.4% of the participants with mild symptoms were below the median (Figure 2).

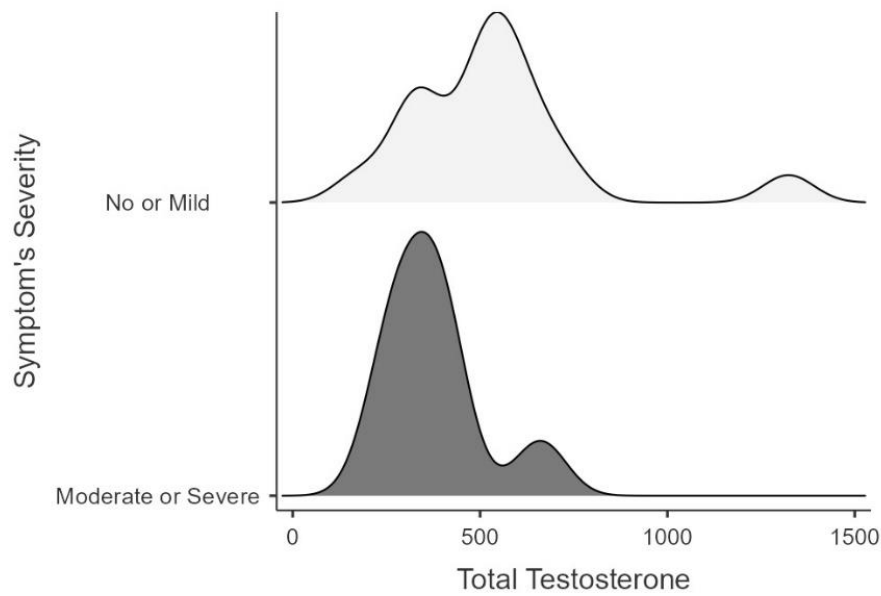


Figure 1 Density plot of total testosterone across no/mild vs. moderate/severe symptoms. *Note: P = 0.07.*

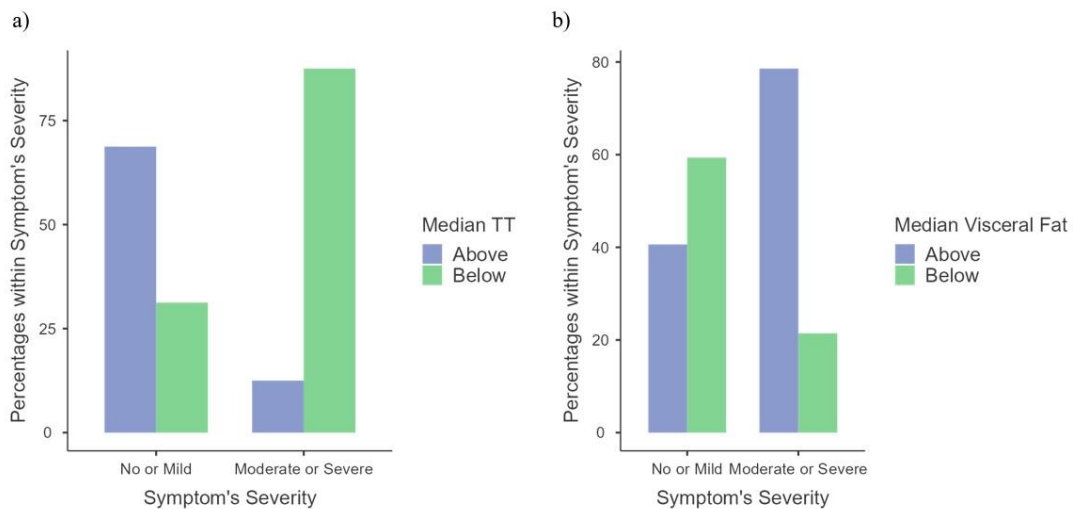


Figure 2 Frequencies (%) of symptom severity, total testosterone and visceral fat. *Notes:* Panel a) Percentage counts of symptom severity and total testosterone. Panel b) Percentage counts of symptom severity and visceral fat.

In addition, although the difference was not statistically significant, most of the individuals who presented moderate/severe symptoms when they had COVID-19 were below the median relative (64.3%) or absolute (57.1%) HGS.

4. Discussion

This study aimed to investigate and compare body composition, muscle strength, and serum testosterone levels in men aged up to 43 years with and without a positive diagnosis of COVID-19 and mild and severe symptoms. The main finding was that the more severe the symptoms were, the lower the testosterone concentration was, even at 12 months after recovery. This result partially confirmed the initial hypothesis. Furthermore, symptom severity was linked to higher visceral fat levels. However, a positive diagnosis or the severity of the symptoms did not impact muscle mass or strength, which does not confirm our alternative hypothesis.

Mean handgrip strength (HGS), a predictor of functional capacity and disability in young and older individuals (Matsudo et al., 2014; Oliveira et al., 2017), was within normal values independent of group classification. Adult males aged 30–40 years typically reach a peak HGS of 41.9 kg/f (Budziareck et al., 2008), whereas study participants presented an average of 41.3 ± 8.3



kg/f when considering the total sample. Similarly, the total testosterone blood concentration in men is expected to be at least 12.1 nmol/L (approximately 349.0 ng/dL) (Al-Zoubi et al., 2021). All median values observed in this study considering group classifications were above this cutoff threshold, with the lowest 25th percentile value of the moderate/severe symptom group being lower than the cutoff value (300.5 ng/dL). Among all participants, the total median testosterone level was 452.0 ng/dL.

One of the initial study hypotheses was that individuals with moderate/severe symptoms would have lower testosterone levels than those with mild or no symptoms. Notably, patients who experienced moderate or severe COVID-19 had the lowest total testosterone levels (32.3% lower than no/mild), with a large effect size, even at 12 months postdiagnosis. This result corroborates existing research showing that moderate or severe COVID-19 can lead to lasting reductions in testosterone, even without necessarily meeting the criteria for androgen deficiency, as in the present sample (Agolli et al., 2021; Karkin & Gürlen, 2022; Nassau et al., 2022). Notably, the reduction can last for up to 80 days (Cannarella et al., 2024), three months (Enikeev et al., 2022), seven months (Salonia et al., 2023), and, from the present data, up to 12 months postinfection.

Individuals with moderate/severe symptoms presented a higher BMI and visceral fat, which aligns with previous findings linking obesity to worse COVID-19 outcomes (Mota et al., 2021; Silva et al., 2021). Although no significant differences in muscle strength were observed between the groups, most of the individuals who presented moderate/severe symptoms when they had COVID-19 were below the median relative (64.3%) or absolute (57.1%) HGS. The same was found among individuals with a positive diagnosis, where more than 60% were below the median absolute and relative HGS. From a clinical point of view, this is a relevant result, as previous studies have shown that patients with greater muscle strength and lean mass recover faster (Gil et al., 2021), whereas COVID-19 has been associated with a significant decline in handgrip muscle strength (Del Brutto et al., 2021).

In the present investigation, age was greater among those diagnosed with COVID-19, which is consistent with epidemiological data. Although the participants were not elderly, the findings align with studies showing that advanced age increases the risk of severe outcomes (Alencar, 2021; Silva et al., 2021). For example, adults under 60 years of age accounted for 33% of COVID-19 deaths in Brazil as of February 7, 2021. It was also observed that volunteers with a positive diagnosis presented significantly less free testosterone (34.8% lower). Although not statistically significant, there were indications of probable clinical relevance for other variables because of size and percentage variations. For example, relative handgrip strength (11.1% lower, medium effect size) and total testosterone (26.0% lower, medium effect size) were lower in men with positive diagnoses, whereas BMI was greater.

This study has several limitations, such as a small sample size, especially for testosterone testing, due to participants' reluctance to perform blood tests, and the use of a convenient sample. Both limitations reduce the statistical power of the analysis. This study did not assess the internal structures of the male reproductive system, unlike some studies involving postmortem biopsies or fertility assessments. However, a notable strength was its pioneering status as the first Brazilian study (to the best of our knowledge) to explore the associations between COVID-19, testosterone, strength, and body composition. The use of dual-energy X-ray absorptiometry (DEXA), the gold standard for body composition analysis, further bolstered these findings.

Future research should incorporate broader functional capacity tests, larger and older samples, and detailed patient records throughout the stages of infection and recovery. Exploring additional variables, such as the impact on male reproductive health and the hypothalamic–pituitary–gonadal axis, would also enhance understanding.

5. Conclusions

In summary, COVID-19 with moderate or severe symptoms is associated with reduced serum testosterone levels, a finding of critical importance for male reproductive health. These results highlight the need to monitor hormonal health in men recovering from COVID-19, ensuring that testosterone levels return to normal. Furthermore, this study highlights the significant relationship between visceral fat and symptom severity. This finding reinforces the importance of obesity prevention as a public health strategy to mitigate adverse outcomes during future pandemics and promote overall health.

Ethical considerations

This study adhered to the ethical standards of Resolution 466/2012 of the Brazilian National Health Council and the Declaration of Helsinki for research involving human subjects. All participants provided informed consent. The institutional ethics committee approved the study (protocol no. 6.812.917/2024).

Conflict of interest

The authors declare that they have no conflicts of interest.

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