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Respiratory muscle sequelae in young university students infected by coronavirus disease 2019: an observational study

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SUMMARY

BACKGROUND: The infection caused by coronavirus disease 2019 can lead to respiratory sequelae in individuals who have experienced severe or mild symptoms.

METHODS: An observational, cross-sectional study was developed, following the STROBE guidelines. Maximal inspiratory and expiratory mouth pressures were assessed in 50 healthy young students (26 women, 24 men; age 22.20±2.41 years). The inclusion criteria were as follows: aged between 18 and 35 years; control group: not diagnosed with coronavirus disease 2019; and coronavirus disease 2019 group: diagnosed with coronavirus disease 2019, at least 6 months ago. The exclusion criteria were as follows: obese/overweight; infected with coronavirus disease 2019 or coronavirus disease 2019 symptoms in the last 6 months; smokers; and asthmatics.

RESULTS: When comparing with groups, the coronavirus disease 2019 group presented statistically significant lower maximal inspiratory pressure values compared with the control group (88.32±16.62 vs. 101.01±17.42 cm H_2O; p=0.01). Regarding the maximal expiratory pressure, no significant differences were found. Similar results were found when performing a subgroup analysis by sex and group.

CONCLUSIONS: Young students who suffered from coronavirus disease 2019 asymptomatically or mildly at least 6 months ago presented a significant decrease in the inspiratory muscle strength as a sequel, so we believe that patients affected by this disease should have a brief postinfection assessment of this musculature to detect the indication for cardiorespiratory rehabilitation.

KEYWORDS: COVID-19. SARS-CoV-2. Students. Complications. Respiratory muscle.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, along with pending massive and effective vaccination globally, is challenging socioeconomic, health, and political systems. The virus enters the respiratory epithelium through the receptor for angiotensin-converting enzyme 2 (ACE2), causing respiratory infection and the well-known acute respiratory syndrome due to coronavirus disease (Sars-CoV-2)[1].

Sars-CoV-2 consists of an acute and sudden respiratory infection of variable course with fever, cough, dyspnea, anosmia, ageusia, muscle aches, diarrhea, chest pain, or headaches[2,3].

In 80% of cases, the symptoms are mild, while 14% present more severe forms with dyspnea, hypoxia, and pneumonia and 5% require admission to intensive care units (ICUs) with respiratory failure and multiorgan failure[4]. Comorbidities, such as obesity, hypertension, chronic obstructive pulmonary disease (COPD), or heart failure, increase mortality. Also, advanced age is the most relevant risk factor for the severity of the illness[5].

Between 40 and 45% of young population do not present symptoms[6]. Also, mortality associated with ages between 20 and 49 years is relatively low, which is around 0.0092%[7]. Even so, healthy young population without associated comorbidities are affected by COVID-19. Studies notify a possible genetic predisposition of these individuals[8].

The infection caused by COVID-19 can lead to respiratory sequelae, but not only in those individuals who have experienced severe forms. It seems increasingly clear that the sequelae are not related to the initial severity of the disease, and although patients who are treated in long-term intensive units suffer from post-ICU syndrome, many young people with mild initial involvement develop sequelae that last for weeks and even months[9].

The sequelae of COVID-19 widely vary, and their manifestations fluctuate between peaks of improvement and clinical worsening. COVID-19 is a multisystemic disease, so its sequelae are very diverse. Lopez-Leon et al. reported that 80% of people who have suffered from COVID-19 present persistent symptoms[7].

In a study carried out in Paris where symptoms were evaluated after an average of 111 days post-COVID-19 infection, the most prevalent symptoms were fatigue (55% of cases), headache (44%), dyspnea (42%), memory loss (34%), concentration and sleep disorders (28%), and hair loss (20%)[10].

Respiratory sequelae of COVID-19 infection are very common, and the most prevalent symptoms are pulmonary

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dysfunction (54% of cases), pleural thickening (27%), polypnea (21%), pain in the chest (16%), and pleural effusion (5%). The published data on persistent dyspnea are quite different, with the prevalence of being 8–43% at 4–8 weeks and 14% at 12 weeks[11].

Most of the data available so far suggest that 10–20% of patients affected by COVID-19 present symptoms 4 weeks after diagnosis. A study carried out in a sample of more than 4,000 people reported persistent symptoms in 13.3% of cases at 4 weeks, 4.5% at 8 weeks, and 2.3% at 12 weeks[12].

Regarding the sequelae described in the young population, the most prevalent symptoms are dyspnea on exertion and physical deconditioning. In this line, Crameri et al. published that VO2max had decreased by >10% in 19% of the 199 military personnel included in the study 45 days after COVID-19 diagnosis[13]. In another sample of 100 participants aged 45–53 years, regardless of the degree of severity of the infection, 60% of population had myocardial involvement and thus dyspnea on exertion[14].

Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) are adequate variables to assess respiratory function. MIP is the pressure generated during maximal inspiratory effort against a closed system. The MEP is measured during a similar maneuver with the total lung capacity[15].

COVID-19 patients who were admitted to ICUs and were assisted by mechanical ventilation later presented general and respiratory hypotonia[16]. However, concerning asymptomatic patients or with mild COVID-19 symptoms, no studies that report respiratory muscle dysfunction are available to date. Due to this reason, and due to the need to establish scientific evidence regarding this new disease, this study aims to assess respiratory muscle function in young patients who have been infected by COVID-19 in a mild or asymptomatic way.

METHODS

Study design

An observational, cross-sectional study was developed, following the STROBE guidelines from March to April 2021 at the Universidad Europea de Madrid.

Settings and participants

A total of 50 healthy young students were recruited at the Universidad Europea de Madrid (26 women, 24 men; age 22.20±2.41 years, height 172.01±7.47 cm, body mass 64.12±8.57 kg). Participants were recruited via email between February and March 2021. They were reassured that nonparticipation had no consequences. A code was assigned to participants before statistical analysis, thus guaranteeing the confidentiality of their data.

The inclusion criteria were as follows: (1) being a student at the Universidad Europea de Madrid; (2) aged between 18 and 35 years; (3) control group (CG): not diagnosed with COVID-19; and (4) COVID-19 group (COVID-G): diagnosed with COVID-19, with a positive polymerase chain reaction (PCR) test, at least 6 months ago.

The exclusion criteria were as follows: (1) obese or overweight; (2) infected with COVID-19 in the last 6 months; (3) smokers; (4) asthmatics; and (5) experienced COVID-19 symptoms in the last 6 months.

Ethical considerations

The current study respected the Declaration of Helsinki ethical statements throughout the study. All the participants read and signed the informed consent form before being part of this investigation.

Measurements

Maximal inspiratory and expiratory mouth pressures (MIP/MEP) were assessed using the Micro Respiratory Pressure Meter (FS985; Micro Medical, Los Angeles, CA, USA). These variables were measured in 25 subjects diagnosed with COVID-19 at least 6 months ago with mild symptoms or asymptomatic, and the same procedure was performed on 25 subjects who had not been ever diagnosed with COVID-19 or had experienced its symptoms.

The Sociedad Española de Neumología y Cirugía Torácica (SEPAR) 2003 procedures manual was followed. The participants rested for 5 min before performing the first maneuver. Then, they performed the maneuvers in a sitting position with a stuffy nose through a clamp that prevented air leaks and a straight back. The examiner showed the maneuver before its performance.

Participants started with MEP: an inspiration was requested at the maximum inspiratory volume with 1 s in inspiratory apnea and then exhaled as hard as possible. The participants rested for 1 min and then repeated the maneuver six times.

Next, MIP was performed. The participants were asked to exhale until the lung was empty, held for 1 s on maximum exhalation, and inhaled as hard as possible. They rested for 1 min between maneuvers until the six maneuvers recommended by the SEPAR were performed.

We recorded the highest value of the MIP and the highest value of the MEP, expressed in centimeter of H_2O.

Regarding anthropometric variables, height (cm; Ano Sayol SL height rod, Barcelona, Spain) and weight (kg; Asimed T2 scale, Barcelona, Spain) were measured. Then, by dividing the weight in kilogram by the height in meters squared, the body mass index (BMI, in kg/m^2) was calculated.

Statistical analysis

A descriptive analysis was developed for all the subjects using mean±standard deviation (SD) to describe the continuous variables. The Shapiro–Wilk test for the normality of the sample was conducted. For nonparametric variables, the Mann–Whitney U test was conducted, while the independent samples t-test was employed to compare the COVID-G with the CG and to determine differences between sex and the remaining of the continuous variables (i.e., MIP, MEP, BMI, age, weight, and height). The significance level was set at alpha <0.017 as three comparisons were performed[17]. All analyses were performed using SPSS version 27.0 statistical software.

RESULTS

Sociodemographic data of the sample

In total, 50 participants (26 women and 24 men), subjects (n=25) in the COVID-G, and subjects (n=25) in the CG were participated in the study. In both groups, 52% of participants were women, and 48% were men. The mean age of the COVID-G was 23.11±2.67 years, the body weight was 67.42±8.77 kg, the height was 174.03±8.07 cm, and the BMI was 22.21±1.50 kg/m^2. The mean age of the CG was 21.32±1.75 years, the weight was 60.80±7.08 kg, the height was 170.04±6.24 cm, and the BMI was 21.13±1.48 kg/m^2. In all these variables, there were significant differences between the two groups, with age, height, weight, and BMI being higher in the COVID-G compared with the CG.

Maximal inspiratory and expiratory mouth pressures

When comparing by groups, the COVID-G presented statistically significant lower values in the MIP, compared with the CG (88.32±16.62 vs. 101.01±17.42 cm H_2O; p=0.01). Regarding the MEP, no significant differences were found between the COVID-G and the CG (105.02±20.41 vs. 103.01±15.83 cm H_2O; p=0.64) (Table 1).

When comparing women by group, there were no statistically significant differences in age, height, weight, and BMI between the COVID-G and the CG. MIP values were lower, with a significant difference, in the COVID-G compared with the CG (75.21±11.60 vs. 88.72±10.61 cm H_2O; p<0.01). Regarding the MEP, no significant differences were found (91.81±20.10 vs. 92.30±11.23 cm H_2O; p=0.94) (Table 1).

Table 1. Subgroup analysis of the maximal inspiratory and expiratory pressures.

Variables	COVID vs. CG	Women: COVID-G vs. CG	Men: COVID-G vs. CG
MIP (cm H_2O)	88.32±16.62 vs. 101.01±17.42*	75.21±11.60 vs. 88.72±10.61*	103.12±5.45 vs. 114.03±13.60*
MEP (cm H_2O)	105.02±20.41 vs. 103.01±15.83	91.81±20.10 vs. 92.30±11.23	120.01±4.42 vs. 114.03±11.61

MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; COVID-G: COVID-19 group; CG: control group. *Significance was set at p<0.017.

When comparing men by group, the COVID-G had a higher height, weight, BMI, and age than the CG, with a statistically significant difference between the variables. MIP values were lower, with a significant difference, in the COVID-G compared with the CG (103.12±5.45 vs. 114.03±13.60 cm H_2O; p=0.016). No significant differences were found in the MEP (120.01±4.42 vs. 114.03±11.61 cm H_2O; p=0.13) (Table1).

DISCUSSION

In this study, the respiratory muscle strength was analyzed in young university students who had COVID-19 mildly or asymptomatically at least 6 months ago. Significantly lower MIP values were observed in the COVID-G compared with the CG, but no significant differences were found in the MEP values.

The COVID-G had significantly higher age, weight, height, and BMI values. Therefore, according to the predictive equations[18,19], the COVID-G should have presented higher MIP and MEP values. As it was not the case, it may be that the COVID-19 infection caused an impairment in the strength of the inspiratory muscles. Nevertheless, in a recent systematic review about predictive MIP and MEP mouth equations, they conclude that there is high heterogeneity in these equations, and none is reliable enough[20].

Comparing by groups and sex, the women of the COVID-G presented lower MIP values than those of the CG, with a statistically significant difference, without finding differences in the MEP. There were no significant differences between the women in both groups in terms of anthropometric variables. Probably, COVID-19 infection caused an impairment in the strength of the inspiratory muscles. Likewise, the men of the COVID-G presented lower MIP values than those of the CG, with a statistically significant difference, despite having a higher weight, age, height, and BMI. No differences were found regarding MEP values.

In patients with respiratory disease, a difference of 7–13 cm H_2O in MIP value is considered clinically significant[21]. In our case, although the population of our study is healthy, the COVID-G subjects presented a similar difference in MIP (being −13.51 cm H_2O in the case of women, or −15%; and −10.91 cm H_2O in the case of men, or −9.5%).

The principal sequelae of COVID-19 infection in the young population described in the literature are VO2max decrease (19% of cases)[13] and myocardial inflammation (60% of cases)[14]. These clinical situations are not correlated with the initial severity of the infection. In our study population, young people between the ages of 18 and 35 years, who had suffered from COVID-19 asymptomatically or mildly at least 6 months ago, presented a clinically significant decrease in inspiratory force[21], a fact that can be related to myocarditis or physical deconditioning, due to the relationship between MIP and VO2max[22].

Since 40–45% of young people affected by SARS-CoV-2 do not present symptoms[6], and the mortality associated with ages between 20 and 49 years is low, around 0.0092%, this population tends to relax barrier measures, has little fear of contagion, and postinfection monitoring is not usually performed. However, the data from this study suggest that young people who have been infected by COVID-19 should undergo an assessment of MIP and MEP, and in case of affectation, they should carry out specific respiratory rehabilitation.

Study limitations and future lines

As a limitation of this study, we could not compare the MIP and MEP values of our population with other reference values using predictive equations, since there are currently none with sufficient reliability[20].

CONCLUSIONS

Although the population of this study is young and experienced an infection by COVID-19 asymptomatically or mildly at least 6 months ago, we found a significant decrease in the inspiratory muscle strength as a sequel. All the patients affected by this disease should have a brief postinfection assessment of this musculature to detect the indication for cardio-respiratory rehabilitation and describe possible sequelae of Sars-Cov-2.

ETHICAL CONSIDERATIONS

The current study was approved by the Research Ethics Committee of Universidad Europea de Madrid and respected the Declaration of Helsinki ethical statements throughout the study. All the participants read and signed the informed consent form before participating in this investigation.

AUTHORS' CONTRIBUTIONS

GGPS: Investigation, Methodology, Formal Analysis, writing – original draft. **MPSF:** Data curation, Investigation, Project administration, Methodology. All authors actively contributed to the discussion of the results in the study and reviewed and approved the final version to be released.

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