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Obesity is associated with a greater number of long-term post-COVID symptoms and poor sleep quality: A multicentre case-control study

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Abstract

Background: Obesity is a risk factor associated with higher mortality at the acute phase of COVID-19; however, its influence on post-COVID symptoms is not known.

Objective: Our aim was to investigate if obesity is a risk factor for the presence of long-term post-COVID symptoms in hospitalised COVID-19 survivors.

Methods: A multicentre case-control study including patients hospitalised during the first wave of the pandemic was performed. Patients with obesity were recruited as cases. Two age- and sex-matched patients without obesity per case were considered as controls. Clinical and hospitalisation data were collected from the hospital medical records. Patients were scheduled for a telephonic interview. A list of post-COVID symptoms was systematically evaluated, but participants were free to report any symptom. Anxiety/depressive levels and sleep quality were evaluated with the hospital anxiety and depression scale (HADS) and Pittsburgh sleep quality index (PSQI), respectively.

Results: Overall, 88 patients with obesity and 176 without obesity were assessed 7.2 months after the hospital discharge. The most prevalent post-COVID symptoms were fatigue and dyspnea. No significant difference in the prevalence of fatigue, dyspnea, anxiety, depression and limitations of daily living activities was observed between people with and without obesity. Obesity was independently associated with a greater number of post-COVID symptoms (IRR 1.56, 95% CI 1.24-1.95, $P < .001$) and poor sleep quality (OR 2.10, 95% CI 1.13-3.83, $P = .02$).

Conclusions: This study found that obesity was associated with a greater number of long-term post-COVID symptoms and poor sleep quality in hospitalised COVID-19 patients.

1 | INTRODUCTION

The rapid worldwide spread of the coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has represented a challenge for healthcare systems. It seems that SARS-CoV-2 disproportionately impacts people with medical comorbidities such as hypertension, obesity, renal insufficiency, or immunosuppressive diseases.[1,2] Obesity has been associated with an increased rate of hospitalisation, worst outcomes and greater lethality.[3]

Healthcare professionals are in front of a second pandemic, the "long-COVID."[4] Current meta-analyses have reported that

almost 80% of COVID-19 survivors will exhibit post-COVID symptoms during the first six months after the infection; however, most published studies had not considered medical comorbidities.[5,6] No previous study has investigated if individuals with obesity are at higher risk of developing more long-term post-COVID symptoms. This is the first study investigating a possible association of obesity with long-term post-COVID symptoms in hospitalised COVID-19 survivors.

2 | METHODS

Patients were classified according to their BMI.

This multicentre study included patients hospitalised for SARS-CoV-2 infection (ICD-10 code) during the first wave of the pandemic (from 1 March 2020 to 31 May 2020) of five public hospitals located in Madrid (Spain). From all hospitalised individuals with a positive diagnosis of COVID-19 by a real-time reverse transcription-polymerase chain reaction (RT-PCR) and also consistent radiological findings, a randomised sample of 300 subjects from each hospital was selected. From these patients, those with an operational definition of obesity (body mass index -BMI- >30 kg/m^2) and previous medical diagnoses were considered. Additionally, two subjects without obesity (BMI <30 kg/m^2) per each case were recruited as controls. Each control was matched by age and sex. If more than two controls per case were available in the same hospital, the selection was randomised. The study was approved by the local Ethics Committee of all hospitals (HUFA 20/126, HUIL/092-20, HUF/EC1517, HSO25112020, HCSC20/495E). All participants provided informed consent before collecting the data.

Clinical and hospitalisation data were collected from the medical records. Participants were scheduled for a telephonic interview by trained healthcare professionals a mean of 7.2 months (SD 0.5) after the hospital discharge. Patients were asked to report the presence of symptoms presented after hospitalisation and persisting at the time of the interview. A systematic list of post-COVID symptoms, eg, dyspnea, fatigue, anosmia, ageusia, chest pain, headache, cough, palpitations, diarrhoea, brain fog, pain or memory loss, was created but they were free to report any symptom that they considered.

Additionally, anxiety/depressive levels and sleep quality were assessed with the hospital anxiety and depression scale (HADS) and the Pittsburgh sleep quality index (PSQI), respectively, as both can be properly administered by telephonic interview.[7] The HADS includes an anxiety (HADS-A, 7-items, 21 points) and a depressive (HADS-D, 7-items, 21 points) symptom subscale.[8] We considered the cut-off scores recommended for the Spanish population (HADS-A ≥ 12 points; HADS-D ≥ 10 points) for determining the presence of anxiety/depressive symptoms, respectively.[9] The PSQI evaluates the quality of sleep over the previous month throughout 19 self-rated questions (total score 0-21).[10] A score ≥8 points suggest poor sleep quality.[10] Functional repercussion was assessed by collecting limitations on daily living activities on occupational activities, social/leisure activities, basic and instrumental activities of daily living.

What's known

- The presence of obesity as medical co-morbidity is associated with higher mortality at the acute phase of COVID-19.
- There is evidence supporting the presence of post-COVID symptoms; however, the role of obesity in the development of these symptoms is not known.

What's new

- This is the first study investigating a possible association of obesity with long-term post-COVID symptoms in hospitalised COVID-19 survivors.
- This multicentre study found a greater number of long-term post-COVID symptoms in individuals with obesity.
- Individuals with obesity also reported poor sleep quality than those without obesity at a long-term follow-up period after the hospital discharge.

Message for the clinic

- This multicentre study shows that people with obesity are at a higher risk of developing long-term post-COVID symptoms and, therefore, early monitoring of these individuals is highly recommended.

The McNemar and paired student's t tests were applied to compare between-groups proportions and means. Multivariable conditional logistic regression models were applied to identify those variables independently associated with obesity. Adjusted odd ratios (OR) or incident rate ratios (IRR) with 95% confidence intervals (95% CI) was calculated.

3 | RESULTS

From 1500 hospitalised patients during the first wave of the pandemic and randomly selected, a total of 88 with obesity were identified. In addition, 176 age- and sex-matched patients without obesity were also recruited. No significant differences in symptoms at hospital admission were observed (Table 1). A significantly greater proportion of patients with obesity also reported hypertension and diabetes when compared with those without obesity (X^2: 35.376, $P < .001$).

From the total sample, 96 (36.4%) were completely free of post-COVID symptoms at seven months after hospital discharge (obesity: n = 20, 22.7%; non-obesity: n = 76, 43.2%, X^2: 23.436, $P < .001$). The number of post-COVID symptoms was significantly higher (IRR 1.51, 95% CI 1.24-1.84, $P < .001$) in patients with obesity (mean: 2.5, SD: 1.6) than in those without obesity (mean: 1.7, SD: 1.3). The most prevalent post-COVID symptoms were fatigue and dyspnea (Table 1). No differences were found in the presence of fatigue (OR

TABLE 1 Demographic, hospitalisation data and post-COVID symptoms of COVID-19 patients with and without obesity

	Obesity group (n = 88)	Non-obesity group (n = 176)
Age, mean (SD), y	52.0 (14.5)	52.2 (14.2)
Sex, male/female (%)	53 (60.2%)/35 (39.8%)	106 (60.2%)/70 (39.8%)
Weight, mean (SD), kg*	101.2 (18.0)	74.0 (13.2)
Height, mean (SD), cm.	169.0 (12.5)	167.0 (10.0)
Body Mass Index, mean (SD), kg/cm^2*	35.5 (5.2)	26.5 (0.75)
Smoking status, n (%)*		
Active	7 (8%)	49 (27.8%)
None or Former	81 (92.0%)	127 (72.2%)
Medical co-morbidities		
Obesity	88 (100%)	0 (0.0%)
Hypertension*	32 (36.7%)	30 (17.0%)
Diabetes*	14 (15.9%)	9 (5.1%)
Cardiovascular disease	10 (11.4%)	21 (11.9%)
Asthma	4 (4.5%)	9 (5.1%)
Migraine	4 (4.5%)	7 (3.9%)
Chronic obstructive pulmonary disease	3 (3.4%)	7 (3.9%)
Other (cancer, kidney disease)	14 (15.9%)	26 (14.8%)
Symptoms at hospital admission, n (%)		
Fever	67 (76.1%)	150 (85.2%)
Dyspnoea	35 (39.8%)	74 (40.1%)
Cough	29 (33%)	50 (28.4%)
Myalgia	27 (30.9%)	50 (28.4%)
Headache	18 (20.4%)	30 (17.1%)
Diarrhoea	12 (13.6%)	16 (9.1%)
Ageusia	3 (9.1%)	6 (5.7%)
Anosmia	8 (9.1%)	18 (10.2%)
Throat Pain	9 (10.3%)	15 (8.5%)
Stay at the hospital, mean (SD), days*	13.2 (10.2)	9.8 (10.69)
Intensive Care Unit (ICU) admission		
Yes/No, n (%)*	9 (10.3%)/79 (89.7%)	7 (4.0%)/169 (96.0%)
Stay at ICU, mean (SD), d*	16.2 (10.6)	6.1 (6.5)
Post-COVID symptoms, n (%)		
Fatigue	58 (65.9%)	103 (58.9%)
Dyspnoea on exertion*	55 (62.5%)	87 (49.7%)
Dyspnoea rest	23 (26.1%)	34 (19.3%)
Memory loss	16 (18.2%)	26 (14.8%)

(Continues)

TABLE 1 (Continued)

	Obesity group (n = 88)	Non-obesity group (n = 176)
Skin rashes*	27 (30.7%)	12 (6.8%)
Gastrointestinal disorders – diarrhoea	8 (9.1%)	18 (10.2%)
Cognitive blunting – brain fog	8 (9.1%)	12 (6.8%)
Concentration loss	12 (13.6%)	16 (9.1%)
Ageusia/hypogeusia	7 (8%)	12 (6.8%)
Ocular/vision disorders*	12 (13.6%)	6 (3.4%)
Tachycardia – palpitations*	11 (12.5%)	8 (4.5%)
Musculoskeletal pain	5 (5.7%)	10 (5.7%)
Anosmia/hyposmia	2 (2.3%)	12 (6.8%)
Migraine-like headache	7 (8%)	10 (5.7%)
Stroke*	7 (8%)	3 (1.7%)

*Significant differences between COVID-19 patients with/without obesity (P < .05).

TABLE 2 Prevalence of functional limitations, anxiety/depressive levels and sleep quality in COVID-19 patients with and without obesity

	Obesity group (n = 88)	Non-obesity group (n = 176)
Functional limitations n (%)		
Limitation in occupational activities	31 (35.2%)	48 (127.4%)
Limitation in leisure/social activities	32 (36.4%)	45 (25.7%)
Limitation in basic activities of daily life	18 (20.4%)	22 (12.6%)
Limitation in instrumental activities of daily life*	30 (34.1%)	38 (21.7%)
HADS-D (0-21), mean (SD)	4.5 (5.0)	4.7 (4.5)
Depressive symptoms (HADS-D ≥ 10 points), n (%)	12 (13.6%)	28 (15.9%)
HADS-A (0-21), mean (SD)	5.1 (5.5)	4.2 (4.6)
Anxiety symptoms (HADS-A ≥ 12 points), n (%)	14 (15.9%)	17 (9.7%)
PSQI (0-21), mean (SD)*	7.2 (4.3)	5.8 (3.6)
Poor sleep quality (PSQI ≥8 points), n (%)*	40 (45.5%)	45 (25.6%)

Abbreviations: HADS, Hospital Anxiety and Depression Scale (A: Anxiety; D: Depression); PSQI, Pittsburgh sleep quality index; SD, standard deviation.

*Significant differences between COVID-19 patients with/without obesity (P < .05).

1.39; 95% CI 0.79-2.43; *P* = .244), dyspnea on exertion (OR 1.41; 95% CI 0.79-2.53; *P* = .243) and dyspnea at rest (OR 1.72; 95% CI 0.99-2.94; *P* = .07) between individuals with and without obesity (Table 1). Similarly, no between-group differences in anxiety (OR 1.75, 95% CI 0.82-3.72, *P* = .146) or depressive (OR 0.83, 95% CI 0.40-1.73, *P* = .628) symptoms were either identified. A higher proportion of patients with obesity (OR 2.27, 95% CI 1.34-3.86, *P* = .002) reported poor sleep quality (Table 2).

From the total sample (n = 264), 119 (45.1%) experienced at least one functional limitation with daily living activities, without between-groups differences (OR 1.61, 95% CI 0.93-2.79, *P* = .085). No differences existed in limitations with occupational activities (OR 1.48, 95% CI 0.83-2.65, *P* = .184), limitations with leisure/social activities (OR 1.67, 95% CI 0.95-2.93, *P* = .075) and limitations with basic activities of daily living (OR 1.68, 95% CI 0.87-3.23, *P* = .121) (Table 2). A greater number of patients with obesity reported limitations with instrumental daily living activities (OR 1.80, 95% CI 1.03-3.15, *P* = .039, Table 2).

The multivariate regression model revealed, after adjusting by all variables, that obesity was independently associated with a greater number of post-COVID symptoms (IRR 1.56, 95% CI 1.24-1.95, *P* < .001) and poor sleep quality (OR 2.10, 95% CI 1.13-3.83, *P* = .02).

4 | DISCUSSION

Identification of patients at a higher risk of developing post-COVID symptoms is crucial for research. To the best of the author's knowledge, this is the first case-control study investigating the association of obesity with long-term post-COVID symptoms. Our study showed that individuals with obesity experienced a greater number of post-COVID symptoms and poor sleep quality in long term than those without obesity. No differences in specific post-COVID symptoms and limitations of daily living activities were found.

Helvaci et al found a pooled prevalence rate of obesity in hospitalised COVID-19 patients of 32% (95% CI 24%-41%).[11] Our prevalence rate was much smaller (n = 88/1500%-6%). It is possible that considering a specific diagnosis by a medical doctor and not just a BMI ≥30 kg/m^2 for being assigned to the case group could explain this discrepancy. As expected, patients with obesity also exhibited comorbid diabetes or hypertension. A meta-analysis has observed that the risk of obesity and diabetes is independent and non-additive between them in COVID-19 patients.[12] These data would suggest that our results are more related to the presence of obesity rather than other comorbidities. In agreement with this hypothesis, the multivariate analysis found that obesity was independently associated with a greater number of post-COVID symptoms and poor sleep quality.

Fatigue and dyspnea were the most prevalent long-term post-COVID symptoms in agreement with the previous meta-analyses supporting that these symptoms are the most prevalent in COVID-19 survivors.[5,6] Wallis et al reported the presence of persistent chest radiograph abnormalities in 32% of hospitalised COVID-19 survivors at 12-week after hospital discharge, findings which would explain the presence of fatigue and dyspnea.[13] These authors also observed that the risk of these persistent abnormalities was associated with obesity.[13]

Obesity was not associated with any particular long-term post-COVID symptom, but these patients exhibited a greater number of symptoms. Since obesity is a multifactorial chronic metabolic disease, it is possible that these patients also exhibit a plethora of post-COVID symptoms to a greater extent than those without obesity. It is possible that multi-systemic, ie, hormonal, metabolic, pro-inflammatory or immune, changes associated with obesity[14] would lead to the developing of the greater number, but not specific, post-COVID symptoms. Nevertheless, obesity was associated with poor sleep quality. However, since obesity is associated with poor sleep quality "per se,"[15] we cannot assume that poor sleep quality is because of COVID-19 since we do not have data before the infection and hospitalisation.

Limitations on daily living activities were not either different between individuals with and without obesity, suggesting that functional limitations seem to be associated with COVID-19. However, since we did not collect the functional status of the patients before the infection, we cannot confirm that these functional limitations are a consequence of COVID-19. In fact, it would be expected that subjects with obesity could exhibit some limitations of daily living activities before infection, and, therefore, these limitations would be related to the obese condition rather than COVID-19. Longitudinal studies are needed to further assess the time course of post-COVID symptoms and functional limitations considering medical co-morbidities.

Our study has some limitations. First, patients were followed up by telephone and not face-to-face. Second, only hospitalised COVID-19 patients were included. Third, we did not collect objective measures of COVID-19 disease, eg, inflammatory biomarkers or serum protein levels. Fourth, we collected data cross-sectionally. Finally, we did not control the medication intake that could have an interaction on post-COVID symptoms.

5 | CONCLUSION

This multicentre study found that obesity was associated with a greater number, but not specific, long-term post-COVID symptoms and poor sleep quality.

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