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Impact of Obesity on Functional and Tomographic Respiratory Sequelae of Patients Hospitalized for COVID-19

Impacto de la obesidad en las secuelas respiratorias funcionales y tomográficas de pacientes hospitalizados por COVID-19

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ABSTRACT

Introduction: Obesity has been recognized as a risk factor for the development of severe forms of COVID-19. However, its impact on long-term functional and tomographic evolution remains a subject of study.

Objective: To evaluate the impact of obesity on the respiratory functional and tomographic evolution of patients hospitalized for COVID-19, with follow-up at 12 months post-discharge.

Materials and methods: A multicenter, prospective, analytical study was conducted on patients hospitalized for moderate and severe COVID-19. Participants were divided into two groups based on their body mass index (BMI): with and without obesity (BMI ≥30 kg/m²). Clinical and functional parameters were evaluated: forced vital capacity (FVC), desaturation during the 6-minute walk test (6MWT), and the presence of a fibrotic pattern on high-resolution computed axial tomography (HRCT) were evaluated at 3, 6, and 12 months.

Results: Of the 78 patients included, 46 (59%) were obese. No statistically significant differences were observed between the groups regarding the evolution of FVC, desaturation during the 6MWT, or the presence of a fibrotic pattern. In the multivariate analysis, obesity was not an independent predictor of tomographic or functional sequelae.

Conclusion: In this cohort, obesity was not associated with a higher prevalence of objective post-COVID-19 respiratory sequelae at 12 months post-hospital discharge. These findings suggest that, once the acute phase of the disease is overcome, the BMI is not a determining predictor of persistent tomographic damage. However, additional studies with much larger samples are required in order to confirm these results.

Key words: COVID-19; hospitalization; obesity; sequelae

RESUMEN

Introducción: La obesidad ha sido reconocida como un factor de riesgo para el desarrollo de formas graves de COVID-19. Sin embargo, su impacto en la evolución funcional y tomográfica a largo plazo sigue siendo motivo de estudio.

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Objetivo: Evaluar el impacto de la obesidad en la evolución funcional respiratoria y tomográfica de pacientes hospitalizados por COVID-19 con seguimiento a los 12 meses del alta.

Materiales y métodos: Estudio multicéntrico, analítico, prospectivo en pacientes hospitalizados por COVID-19 moderado y grave. Los participantes fueron divididos en dos grupos según índice de masa corporal (IMC) con y sin obesidad (IMC ≥30 kg/m²). Se evaluaron parámetros clínicos, funcionales: capacidad vital forzada (CVF), desaturación durante la prueba de caminata de 6 minutos (PC6M); y presencia de patrón fibrótico en TACAR a los 3, 6 y 12 meses.

Resultados: De los 78 pacientes incluidos, 46 (59%) presentaban obesidad. No se observaron diferencias estadísticamente significativas entre los grupos en cuanto a la evolución de CVF, la desaturación en la PC6M o presencia de patrón fibrótico. En el análisis multivariado, la obesidad no fue un predictor independiente de secuelas tomográficas ni funcionales.

Conclusión: En esta cohorte la obesidad no se asoció a una mayor prevalencia de secuelas respiratorias objetivas post-COVID-19 a los 12 meses del alta hospitalaria. Estos hallazgos sugieren que, una vez superada la fase aguda de la enfermedad, el IMC no es un predictor determinante de daño tomografico persistente. No obstante, se requieren estudios adicionales con muestras más grandes para confirmar estos resultados.

Palabras claves: COVID-19; hospitalización; obesidad; secuelas

INTRODUCTION

The COVID-19 pandemic has had a significant impact on global public health, not only during its acute phase but also due to the sequelae that may persist months after the initial infection.[1-4] Various studies have identified obesity as a risk factor for developing severe forms of the disease, with a higher risk of hospitalization, admission to Intensive Care Units, and mortality. This has been attributed to a chronic inflammatory state, immune dysfunction, and ventilatory mechanical alterations associated with excess adipose tissue.[5,6]

While the role of obesity in the acute phase is well established, its influence on long-term recovery remains an area of active research. Some studies indicate that once the critical phase has been overcome, the BMI does not necessarily predict the presence of objective pulmonary sequelae.[7-11]

The objective of this study is to analyze whether obesity affects the functional and tomographic evolution of patients hospitalized for moderate and severe COVID-19, with outpatient follow-up for up to 12 months after hospital discharge.

MATERIALS AND METHODS

Descriptive, analytical, prospective, multicenter study (Hospital A. Posadas, Hospital Ramos Mejía, Hospital F. Santojanni, Hospital Churruca-Visca. Secuelar-19 Study). The study was approved by the Ethics and Research Committee of each participating hospital. All patients signed informed consent.[12,13]

The study included adult patients hospitalized in general wards or in the Intensive Care Unit (ICU) for moderate or severe COVID-19, confirmed by nasal swab, between June 1, 2020, and April 9, 2021. Outpatient follow-up was conducted with evaluations at 3, 6, and 12 months after hospital discharge.

The following data were recorded: clinical data (age, sex, BMI), comorbidities, hospitalization in general ward or ICU and requirement of mechanical ventilatory assistance, functional parameters (FVC, oxygen desaturation during 6MWT), tomographic parameters (presence of a fibrosis-like pattern on HRCT).

The following operational definitions were used for the variables evaluated:

Moderate COVID-19 disease (Cao category 4): defined as disease requiring hospitalization in a general ward with a PaO_2/FiO_2 ratio greater than 200, without signs of sepsis and/or hemodynamic instability. Severe COVID-19 disease (Cao categories 5-6): defined as disease requiring hospitalization in the ICU, intermediate care, or ward requiring NG support, with a PaO_2/FiO_2 ratio less than 200, and signs of sepsis and/or hemodynamic instability.

Six-Minute Walk Test (6MWT): performed according to the criteria established by the 2009 Guidelines of the ATS/ERS (American Thoracic Society/European Respiratory Society). "Desaturating patients" (DP) were defined as those with a drop of ≥4 percentage points in oxygen saturation (SaO_2) during the 6MWT. "Non-desaturating patients" (NDP) were defined as those who did not reach this threshold.

HRCT imaging: a fibrotic-like HCRCT pattern was defined as the presence of at least one of the following tomographic findings: interlobular septal thickening,

reticulations, traction bronchiectasis, and/or honeycombing.[21] A non-fibrotic pattern was defined by the following tomographic signs: ground-glass opacities (GGOs), crazy paving, nodules, and alveolar consolidation.[14]

Analysis groups: patients with obesity (BMI ≥ 30 kg/m²) and non-obese patients (BMI < 30 kg/m²).

Statistical analysis: categorical variables were reported as frequency and percentage. Continuous variables that assumed a normal distribution were reported as mean and standard deviation (SD). Otherwise, the median and interquartile range (IQR 25-75%) were used. To compare continuous variables between independent groups, the Student's T-test or the Mann-Whitney U test was used, as appropriate. For the comparison of categorical variables, the Chi-square test or Fisher's exact test was used, as appropriate.

To estimate the odds ratios (ORs) and 95% confidence intervals (95% CI) for the association between obesity and different outcome variables –fibrosis-like pattern on HRCT, forced vital capacity < 80%, and desaturation during the 6MWT at 12 months– adjusted multiple logistic regression models were used.

Demographic variables, respiratory functional parameters, and imaging findings were analyzed by comparing the obese and non-obese groups.

An online data collection platform was used (www.mawetools.com). A p value < 0.05 was considered statistically significant. Data analysis was performed using SPSS® for Macintosh software, version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

In the SECUELAR-19 study, 111 of 305 patients were excluded for various reasons.

At the 12-week analysis, 194 participants were included; 129 (66.5%) continued after 6 months of follow-up, and 103 (53%) completed the study up to week 52. 78 of those patients were included in the present study because they had complete data on obesity status, of whom 46 (59%) were obese.

Table 1 shows the demographic and clinical variables at study admission for obese and non-obese patients. Patients with obesity were predominantly female (p = 0.036) and had a higher prevalence of arterial hypertension (p = 0.016). Patients with a history of smoking (former/current smoker) accounted for 33% of the sample (26 patients).

In the functional evaluation at 3, 6, and 12 months, no significant differences were observed between the two groups in terms of FVC or desaturation during the 6MWT.

The fibrosis-like tomographic pattern was frequent at baseline (greater than 50%) and then progressively decreased in both groups, without significant differences (Table 2). (Fig.1).

In contrast, the presence of FVC < 80% at 3 months showed a strong association with the persistence of fibrotic patterns on CT.

DISCUSSION

This study has shown that in this cohort, obesity was not associated with a higher prevalence of tomographic post-COVID-19 sequelae at 12 months after hospital discharge.

In the SECUELAR-19 study, improvement was observed in all variables when comparing the evaluations at 3, 6, and 12 months. However, functional and tomographic abnormalities persisted after one year, with a fibrosis-like tomographic pattern in 35%, reduced FVC in about one quarter of patients, and desaturation in 12.8% of patients.[12,13]

Regarding tomographic findings, Athon Wells questioned whether the fibrotic-like pattern truly indicates irreversible damage in a lung recovering from acute respiratory distress syndrome (ARDS), as the "honeycomb" sign typically does. He also questioned the non-fibrotic–like pattern described

TABLE 1. Basal characteristics of participants 3 months after hospital discharge

Variables	All (n=78)	Obese (n=46)	Non- Obese (n=32)	P value
Age, mean (SD)	56.2 (9.1)	56.9 (9.2)	55.2 (9.0)	0.41
Females, n (%)	25 (32.1%)	19 (41.3%)	6 (18.8%)	0.036
BMI, median (IQR)	30 (28-34)	33 (31-36)	26.5 (25-28)	<0.001
Desaturation after 3 months, n (%)	25 (32.1%)	15 (32.6%)	10 (31.3%)	0.90
FVC < 80% after 3 months, n (%)	29 (37.2%)	15 (32.6%)	14 (43.8%)	0.32
Charlson Index, median (IQR)	2 (1-3)	1 (1-3)	2 (1-3)	0.24
History of respiratory diseases, n (%)	13 (16.7%)	7 (15.2%)	6 (18.8%)	0.68
Arterial hypertension, n (%)	24 (30.8%)	19 (41.3%)	5 (15.6%)	0.016
Diabetes, n (%)	22 (28.2%)	11 (23.9%)	11 (34.4%)	0.31
Requirement of MVA, n (%)	25 (32.1%)	11 (23.9%)	14 (43.8%)	0.065
Severe pneumonia, n (%)	42 (53.8%)	25 (54.3%)	17 (53.1%)	0.91

TABLE 2. Evolution of the fibrotic-like pattern on CT by group

Follow-up time	Non- Obese (n=32)	Obese (n=46) p-value	p-valor
SF a los 3 meses	19 (59.4%)	24 (52.2%)	0.691
SF a los 6 meses	13 (40.6%)	14 (30.4%)	0.491
SF a los 12 meses	11 (34.4%)	13 (28.3%)	0.744

CT: computed tomography Chi²: square Chi test.
No statistically significant differences were found between groups at any of the time points evaluated (p > 0.05).

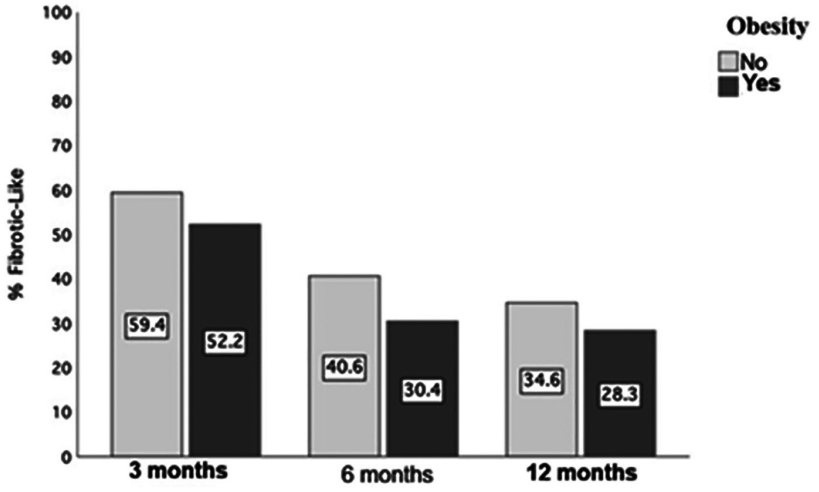

Figure 1. Evolution of the fibrotic-like pattern on CT by group

TABLE 3. Logistic regression analysis: factors associated with the fibrotic-like pattern

Variable	OR (95% CI)	p value
Age	1.058 (1.016 - 1.102)	0.006
Males	0.949 (0.415 - 2.171)	0.902
Obesity	0.705 (0.338 - 1.470)	0.351
Severe pneumonia	1.467 (0.718 - 2.997)	0.293
Predicted FVC <80% (3 months)	3.873 (1.732 - 8.661)	0.001
Desaturation (3 months)	1.205 (0.531 - 2.734)	0.656

by Han et al, noting that ground-glass opacities can sometimes indicate irreversible interstitial fibrosis in other interstitial lung diseases. In this clinical context, lung injury may be mediated by viral pathogenicity, but it may also be related to lung injury induced by mechanical respiratory assistance (MRA). Other mechanisms of viral lung injury have also been proposed, including autoimmune-mediated inflammation and vascular damage. It has also been suggested that 5–10% of adults have pre-existing lung diseases, and that mechanical ventilation in ARDS can leave residual imaging abnormalities for up to a year, further complicating the interpretation of lung imaging.[15]

Several international studies have shown that obesity is a significant risk factor for an unfavorable course during the acute phase of COVID-19, with a higher risk of hospitalization, admission to the Intensive Care Unit, mechanical ventilation, and mortality. These effects are explained by several pathophysiological mechanisms, including reduced respiratory functional capacity due to mechanical limitations, immune dysfunction induced by adipose tissue, and the chronic pro-inflammatory state characteristic of obesity. [7-11]

Our study, however, focuses on long-term outcomes and found that in patients who survived the acute phase and underwent structured outpatient follow-up, obesity was not significantly associated with functional or tomographic respiratory sequelae at 12 months after discharge.

A recent systematic review found that obese patients had a higher prevalence of persistent symptoms, including dyspnea, fatigue, and cognitive impairment, as well as reduced functional capacity in exercise testing.[16,17] Studies using cardiopulmonary exercise testing have shown that post–COVID-19 obese patients present abnormalities in gas exchange and an abnormal ventilatory response, including inefficient hyperventilation and reduced peak oxygen consumption. This supports the hypothesis that functional impairment is not always detectable by standard testing.[18]

Our findings align with the SECUELAR-19 study conducted in Argentina, which identified diabetes, pre-existent respiratory disease, and early fibrotic pattern on HRCT as factors associated with persistent functional impairment–not implicating obesity.[17] This consistency suggests that once the acute phase has been overcome, BMI *per se* does not necessarily predict lasting structural lung damage.

Among the limitations of the present study are the small sample size, the lack of stratification by obesity class (I, II, III), and the absence of baseline functional data prior to COVID-19 infection. Additionally, metabolic variables and factors such as vaccination status or viral variants –which could have influenced outcomes– were not evaluated.

Despite these limitations, the results provide relevant local evidence indicating that obesity, in the context of protocolized follow-up, is not associated with a higher prevalence of objectively measurable long-term pulmonary sequelae. Larger prospective studies including body composition measurements, inflammatory markers, and cardiopulmonary exercise testing are required to better clarify the impact of post-COVID obesity.

Conflict of interest
None to declare

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