

# **SARS-COV-2 INFECTION IN PATIENTS OPERATED BY BARIATRIC SURGERY: A LITERATURE REVIEW**

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**Abstract:** In less than a year, the SARS-CoV-2 pandemic has become responsible for more than 2 million deaths worldwide, leading to the disruption of all health systems and economic disasters. There is now clear evidence that severe obesity is a significant risk factor for mortality. Patients are generally healthier after metabolic surgery, which can result in a less severe form of SARS-CoV-2 infection and a better prognosis after contracting this disease. To test this hypothesis, the present study was designed to determine the association of previous metabolic surgery with the severity of SARS-CoV-2 infection in severely obese patients. Non-systematic literature review study in the Medline scientific database focusing on the association between previous metabolic surgery and COVID-19 severity in obese patients. The findings of this review of 7 observational studies in patients with a history of prior bariatric surgery indicate that a history of bariatric surgery is associated with lower rates of hospitalization and mortality in obese patients after SARS-CoV-2 infection. The present study revealed that findings from observational studies suggest that prior bariatric surgery is associated with a lower rate of mortality and hospital admission in obese patients who become infected with SARS-CoV-2. Confirmation of these findings will require larger studies with better quality data.

**Keywords:** Bariatric surgery, COVID-19, Coronavirus, Diabetes, Metabolic surgery, Obesity, SARS-CoV-2, Weight loss.

## INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic started in Wuhan province, China, spreading globally and impacting countries in different ways. The world has more than 190,375,116 cases, 4,088,293 deaths and about 2 billion (13.40% of the population) fully vaccinated

people (as of July 22, 2021). Brazil had its first case of COVID-19 on February 25, 2020 (BURKI et al. 2020), and has since faced 22,529,183 cases, 620,251 deaths and 335,742,922 fully vaccinated people (as of January 10, 2021). (DONG et al. 2021).

In less than a year, the SARS-CoV-2 pandemic has become responsible for more than 2 million deaths worldwide, leading to the disruption of all health systems and economic disasters. There is now clear evidence that severe obesity is a significant risk factor for mortality independently of diabetes, chronic kidney failure and cancer in patients with SARS-CoV-2 (CZERNICHOW et al. 2020; BEL LASSEN et al. 2021). In this context, the percentage of body fat is expressed as the Body Mass Index (BMI), which is commonly used to classify underweight, overweight or obesity in adults and children. BMI is calculated as the ratio of body weight to body height, measured in kilograms (kg) and square meters (m<sup>2</sup>), respectively (Smith et al. 2016). A BMI above 25 is considered overweight and above 30 is obese. these values are the same for both sexes and for all ages of adults. The definition of overweight or obesity depends on the age of the child population. Overweight and/or obesity is a chronic disease characterized as an abnormal and excessive amount of body fat that can impair the immune system (FUENZALIDA et al. 2016; KELISHAD et al. 2017). In 2016, it was estimated that more than 1.9 billion adults (≥18 years of age) worldwide were overweight and more than 650 million were obese.

Bariatric surgery (BC) is the only effective long-term treatment for severe obesity (ADAMS et al. 2018). Indeed, metabolic surgery (defined as procedures that influence metabolism by inducing weight loss and altering gastrointestinal physiology) leads to substantial and sustained weight loss; improvement in cardio-metabolic risk factors,

including diabetes and blood pressure control; reduced risk of major adverse cardiovascular events; improvement of cardiopulmonary and renal functions; improvement of the pro-inflammatory state associated with obesity; and survival benefits in severely obese patients.

During the first wave of SARS-CoV-2, CB activity almost completely stopped for several months. One of the reasons given was that a recent BC could expose obese patients to the risk of a severe form of SARS-CoV-2 due to massive weight loss, transient immune dysfunction, or vitamin and mineral deficiencies, which are frequent during the first year following to CB. Patients are generally healthier after metabolic surgery, which can result in a less severe form of SARS-CoV-2 infection and a better prognosis after contracting this disease. To test this hypothesis, the present study was designed to determine the association of previous metabolic surgery with the severity of SARS-CoV-2 infection in severely obese patients.

## **JUSTIFICATION**

Today, overweight and obesity kill more people in developed countries than underweight in developing countries. At least 2.8 to 4 million deaths per year are recorded as resulting from incipient overweight and morbid obesity (W.H.O. 2021). Excess weight was recorded in 39% of men and 40% of women in the adult population; in addition, 11% of men and 15% of women were obese. More than 340 million children (5–18 years) were overweight and obese in 2016 (WHO et al. 2021). According to 2019 statistics, the prevalence of overweight and obesity in children has increased significantly, with around 40 million patients under 5 years of age (Di et al. 2019). It is predicted that nearly 50% of the world's population will become obese by 2050.

Obesity can represent a serious health risk factor and is often linked to the development of chronic inflammatory diseases, for example, type 2 diabetes, hypertension, cardiovascular disease, chronic lung disease and cancer (KYROU et al. 2018; ZHOU et al. 2020; WU et al. 2020). These comorbidities are associated with a severe clinical course of respiratory infection caused by influenza virus and SARS-CoV-2 infection. As a serious health risk factor, obesity leads to more frequent hospitalizations and increases morbidity and mortality worldwide compared to non-obese individuals (SMITH et al. 2016). Childhood obesity is mainly associated with a worse course of respiratory diseases (FUENZALIDA et al. 2016).

## **GOALS**

### **MAIN GOAL**

To investigate the incidence of SARS-CoV-2 infection and its severity in patients undergoing bariatric surgery.

### **SPECIFIC OBJECTIVES**

To report whether Sars-Cov-2 infection and morbidity/mortality related to laparoscopic BC; and secondary outcomes such as readmission and reoperation rates.

### **METHOD(S)**

A non-systematic literature review study carried out until January 10, 2022. The search terms were: "COVID-19" OR "SARS-CoV-2" AND "bariatric" OR "RYGB" OR "gastric bypass" OR "sleeve" in the Medline scientific database (via PubMed). As technical procedures, bibliographic and survey research was used, which aims to put the researcher in contact with the literature made public by other researchers through scientific articles, dissertations, theses, among others. Articles originally published in English were considered eligible. Articles published in the

databases from 2020 to 2022 were included, focusing on the guiding question: is there an association between previous metabolic surgery and severity of COVID-19 in patients with obesity? The main inclusion criteria were full articles freely available; articles in English; clinical trials, randomized controlled trials and systematic literature reviews. The exclusion criteria were: duplicate articles and articles outside the topic addressed

## RESULTS

Recently, among 4,365 patients who tested positive for SARS-CoV-2 between March 8, 2020 and July 22, 2020 at the Cleveland Clinic Health System, 33 patients with a prior history of metabolic disease were identified. Surgical patients had a 1:10 propensity to non-surgical patients to assemble a cohort of control patients ( $n = 330$ ) with  $BMI \geq 40 \text{ kg/m}^2$  at the time of the SARS-CoV-2 trial. The primary outcome was the hospital admission rate. Secondary outcomes included admission to the ICU unit, need for MV and dialysis during the index hospitalization, and mortality. The large study revealed that the mean BMI of the surgical group was  $49.1 \pm 8.8 \text{ kg/m}^2$  before metabolic surgery and dropped to  $37.2 \pm 7.1$  at the time of SARS-CoV-2 testing compared to with the BMI of the control group of  $46.7 \pm 6.4 \text{ kg/m}^2$ . In the univariate analysis, 6 (18.2%) patients in the metabolic surgery group and 139 (42.1%) patients in the control group were admitted to the hospital ( $P = 0.013$ ). In multivariate analysis, a prior history of metabolic surgery was associated with a lower rate of hospitalization compared with obese control patients (odds ratio, 0.31; 95% confidence interval, 0.11-0.88;  $P = 0.028$ ). While 43 (13.0%) patients in the control group required ICU admission ( $P = 0.021$ ), 22 (6.7%) required MV, 5 (1.5%) required dialysis, and 8 (2, 4%) patients died (AMINIAN et al. 2021).

In another study, we retrospectively analyzed data from electronic medical records of 6,700 PCR-positive adults for SARS-CoV-2 from March 1, 2020 to August 25, 2020. Logistic regression and competitive risk were used to assess the odds of hospitalization. Additional adjustment was added to assess risk of hospitalization among patients prescribed metformin use in the 3 months prior to SARS-CoV-2 PCR result, history of home use of glucagon-like peptide 1 (GLP-1) receptor agonist RA), and history of metabolic and bariatric surgery. Interactions were assessed by gender and race. It was observed that a history of NAFLD/NASH was associated with greater odds of admission for Covid-19: logistic regression OR 2.04 (1.55, 2.96,  $p < 0.01$ ), concurrent risks OR 1.43 (1.09–1.88,  $p < 0.01$ ); and each additional year of NAFLD/NASH was associated with a significantly increased risk of being hospitalized for Covid-19, OR 1.86 (1.43–2.42,  $p < 0.01$ ). After controlling for NAFLD/NASH, people with obesity were less likely to be hospitalized for Covid-19, OR 0.41 (0.34–0.49,  $p < 0.01$ ). NAFLD/NASH increased the risk of hospitalization in men and women, and in all racial/ethnic subgroups. Mediation treatments for metabolic syndrome were associated with a non-significant reduced risk of admission: OR 0.42 (0.18–1.01,  $p = 0.05$ ) for metformin home use and OR 0.40 (0.14–1.17,  $p = 0.10$ ) for domestic use of GLP-1 RA (BRAMANTE et al. 2020).

An article conducted through obese patients hospitalized by France's National Health Insurance had their electronic health data reviewed retrospectively. Patients undergoing BC comprised the BC group and patients with obesity but without a history of BC served as controls. The primary endpoint was COVID-19-related death and the secondary endpoint was the need for Invasive Mechanical Ventilation (IMV). It was observed that 4,248,253 obese

individuals aged 15-75 years were included and followed up for a mean observation time of  $5.43 \pm 2.93$  years. 8,286 individuals with a previous diagnosis of obesity were admitted for COVID-19 between January 1 and May 15, 2020. Of these patients, 541 had a history of BC and 7,745 did not. The need for IMV and death occurred in 7% and 3.5% of the CB group versus 15% and 14.2% of the control group, respectively. In logistic regression, IMV risk was independently associated with increasing age, male sex, and hypertension, and mortality was independently associated with increasing age, male gender, history of heart failure, cancer, and diabetes, whereas BC had an effect. independent protective effect. Two random exact match tests confirmed the protective effect of BC (IANNELLI et al. 2021).

The Cleveland Clinic and University of Minnesota studies independently reported a lower risk of hospitalization in patients with prior bariatric surgery after contracting SARS-CoV-2 infection. All 3 studies reported the mortality outcome (IANNELLI et al. 2021; AMINIAN et al. 2021; BRAMANTE et al. 2020). The risk of mortality without prior bariatric surgery was 133 per 1000 cases and its risk with prior bariatric surgery was 33 per 1000 (summary OR 0.22, 95% CI 0.19–0.26, based on meta-analysis of random effects).

The cohort study was the database of the Program de Médicalisation des Systèmes d'Information. This database contains all diagnoses coded using ICD-10 in a public or private hospital in France. This cohort study was declared to the French Data Protection Authority (MR-005, n° 5714251020). All patients suffering from obesity and undergoing BS between January 1, 2015 and December 31, 2019 are included, combining bariatric surgery procedure codes and ICD-10 E66 (overweight and obesity) codes. For these patients, we identified all admissions diagnosed with

SARS-COV-2 between January 1, 2020 and August 31, 2020, identified by the following ICD-10 codes: U0710, U0711, U0712, U0714, U0715. For all included patients, classes (BMI) ( $[40-50]$ ,  $\geq 50 \text{ kg/m}^2$ ), high blood pressure diagnostic codes (I10) and diabetes codes (E11) are extracted at the time of hospitalization for infection of the SARS-COV-2. It turned out that a total of 227,681 patients were hospitalized for a BC in France. Among them, 477 (2.1 per 1000 patients) were hospitalized for SARS-CoV-2 infection between January 1, 2020 and August 31, 2020. Hypertension (OR = 1.4 [1.2; 1.6],  $p < 0.001$ ) and diabetes (OR = 1.5 [1.2; 1.9],  $p = 0.002$ ) at the time of BS significantly increased the risk of hospitalization for SARS-CoV-2. A BMI greater than  $50 \text{ kg/m}^2$  at the time of BC was not associated with the risk of hospitalization. Likelihood of being hospitalized for SARS-COV-2 significantly increases with CB date: 2020 age-standardized hospitalization risk was significantly reduced for patients with CB in the past 2 years compared to those who had more remote CB (POGHOSYAN et al. 2021).

One article carried out a questionnaire to patients who had already undergone bariatric surgery by telemedicine and educational videos for obese and bariatric patients. A total of 2145 patients (313 men; 1832 women) responded to the questionnaire. It was observed that the mean pre-surgical BMI:  $44.5 \pm 6.8 \text{ kg / m}^2$ . Mean age:  $44.0 \pm 10.0$  years. Mean BMI after surgery:  $29.3 \pm 5.5 \text{ kg / m}^2$  ( $p < 0.05$ ). From February to May 2020, 8.4% of patients reported that they suffered from at least one symptom among those identified as related to SARS-CoV-2 infection. Thirteen patients (0.6%) tested positive for COVID-19. Six patients (0.3%) were admitted to the COVID Department and 2 patients (0.1%) were admitted to the ICU (UCCELLI et al. 2021).



In another study conducted from April to August 2020, 594 patients from 6 large bariatric centers in Italy received an 87-item telephone questionnaire. Demographic data, COVID-19 incidence, suggestive symptoms, and clinical outcome parameters of operated patients and CB candidates were compared. The incidence of symptomatic COVID-19 was evaluated including the clinical definition of probable case, according to World Health Organization criteria. 353 operated patients and 169 CB candidates were finally included in the statistical analysis. While the incidence of COVID-19 confirmed by laboratory tests was similar in the two groups (5.7% vs 5.9%), lower incidence of most symptoms related to COVID-19, such as anosmia (p: 0.046), dysgeusia (p: 0.049), rapid onset fever (p: 0.046) were recorded among operated patients, resulting in a lower rate of probable cases (14.4% vs 23.7%; p: 0.009). Hospitalization was frequent in patients who were candidates for BC (2.4% vs 0.3%, p: 0.02). One death in each group was reported (0.3% vs 0.6%). Pneumonia and previous neoplasms were associated with symptomatic COVID-19 in univariate and multivariate analysis (MARCHESI et al. 2021).

## DISCUSSION

As more evidence develops, patients with obesity are disproportionately affected by SARS-CoV-2 infection. This study suggests that a history of metabolic surgery is associated with lower severity of SARS-CoV-2 infection in patients with severe obesity, manifested by lower risks of hospital and ICU admission. The findings of this review of 7 observational studies in patients with a history of prior bariatric surgery indicate that a history of bariatric surgery is associated with lower hospitalization and mortality rates in obese patients after contracting SARS-CoV-2 infection.

Several studies from the United States, Europe, and China have consistently reported adverse clinical outcomes, including higher rates of hospitalization, severe pneumonia, ICU admission, need for invasive mechanical ventilation, and mortality in obese patients who develop COVID-19 (DOCHERTY et al. 2020; ROTTOLI et al. 2020; CACI et al. 2020). The results of the present study suggest that metabolic surgery provides substantial and durable weight loss and an improved overall health profile that may lead to better outcomes in patients with SARS-CoV-2 infection. Metabolic abnormalities, including type 2 diabetes and hypertension, were significantly improved after metabolic surgery in most surgical patients. Although the sample size was small, none of the surgical patients experienced ICU admission, mechanical ventilation, dialysis, or death after contracting SARS-CoV-2 infection. As a pro-inflammatory and prothrombotic disease process, the effects of SARS-CoV-2 infection can be counteracted by metabolic surgery aimed at improving the obesity-mediated inflammatory response. Reducing excess adipose tissue reduces the inflammatory response, enhances immunity, and improves the physiology and mechanics of the lungs and chest wall. Furthermore, improvements in cardio-metabolic risk factors after surgically induced weight loss may contribute to better outcomes for obese patients who have had prior metabolic surgery.

The COVID-19 pandemic has highlighted the vulnerabilities of patients with obesity and the need to create better strategies for managing this chronic disease process (SILECCHIA et al. 2021). Efforts to address the obesity epidemic will help improve not only the overall health of the individual, but also the health of a society, having the greatest impact on improving health outcomes in a vulnerable population. By rapidly addressing

Author	Year	Goal	Conclusion
Aminian et al.	2021	To investigate the relationship between prior metabolic surgery and the severity of COVID-19 in severely obese patients.	Prior metabolic surgery with subsequent weight loss and improvement of metabolic abnormalities was associated with lower hospital and ICU admission rates in obese patients who became infected with SARS-CoV-2. Confirmation of these findings will require larger studies.
Silecchia et al.	2021	To analyze the results of any Sars-Cov-2 infection and related morbidity/mortality at 30 days after laparoscopic BC during phase 2-3; secondary outcomes were readmission and reoperation rates.	The introduction of strict COVID-19 protocols regarding the protection of patients and healthcare professionals has ensured a safe resumption of elective CB in Italy. The safety profile was also maintained during the second wave of the outbreak, thus allowing access to a cure for the obese population.
Iannelli et al.	2021	To determine the risk of invasive mechanical ventilation and death in obese individuals with a history of bariatric surgery (BC) admitted for COVID-19.	This national study showed that BC is independently associated with a reduced risk of death and invasive mechanical ventilation in obese individuals with COVID-19.
Marchesi et al.	2021	To investigate the incidence of SARS-CoV-2 infection and its severity in patients undergoing bariatric surgery.	Patients undergoing BC appear to develop less severe SARS-CoV-2 infection than obese individuals.
Poghosyan et al.	2021	To investigate the association between the time of bariatric surgery and the risk of hospitalization for SARS-CoV-2.	This cohort study showed that patients who had recent bariatric surgery were not at increased risk of hospitalization in case of SARS-CoV-2 infection. Further prospective studies will help to unravel this complex question.
Uccelli et al.	2021	To investigate the incidence of SARS-CoV-2 infection and its severity in patients undergoing bariatric surgery.	Although reported rates of symptoms and fever were high, only 0.6% of patients tested positive for COVID-19. Among the more than 2,000 patients undergoing bariatric surgery analyzed in this study, only 0.1% required ICU admission.
Bramante et al.	2020	Covid-19 disease causes significant morbidity and mortality through increased inflammation and thrombosis. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis are states of chronic inflammation and indicate advanced metabolic disease. We seek to understand the risk of hospitalization for Covid-19 associated with NAFLD/ NASH.	NAFLD/NASH is a significant risk factor for hospitalization for Covid-19 and appears to be responsible for the risk attributed to obesity. Treatments for metabolic diseases reduced NAFLD/NASH risks. More research is needed to confirm the risk associated with visceral adiposity, and patients mus0074 be screened and informed about treatments for metabolic syndrome.

Table 1: Conclusion and objective of included patient studies

obesity in our community, we can prevent the immediate health effects associated with obesity in addition to the heightened risks associated with unforeseen local or global health scares (DICKER et al. 2020; LE BROCCQ et al. 2020; BORNSTEIN et al. 2020).

The results of the current study suggest that patients with obesity and metabolic diseases become healthier after bariatric surgery and may better fight off SARS-CoV-2 infection. If these findings are confirmed in future mechanistic and clinical studies, better clinical outcomes from COVID-19 could be added to the long list of health benefits of bariatric surgery (AMINIAN et al. 2021).

This study is one of the few literature reviews that reports the possible protective effects of bariatric surgery in patients with COVID-19 infection. As this study was performed based on data originating from the COVID-19 pandemic, there are several limitations. Due to the small number of studies and the lack of high-quality data, any strong conclusions about the protective effects of bariatric surgery after contracting SARS-CoV-2 infection in obese patients seems premature. Considering these limitations, the findings of this review must be interpreted with caution and considered as generating hypotheses.

## CONCLUSION

In summary, the present study revealed that findings from observational studies suggest that prior bariatric surgery is associated with a lower rate of mortality and hospital admission in obese patients who become infected with SARS-CoV-2. Confirmation of these findings will require larger studies with better quality data.

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