



## Is Bariatric Surgery Contributing to a Decreasing Trend in Covid-19 Infection and Complication Rate in Obese Patients ?

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**Abstract:** The objective of this study is to identify bariatric surgery as a treatment modality to reduce Covid-19 related morbidity, mortality and complication rate in the obese patients. This study involves the comparison of 2 researches in which Covid-19 affected patients were assessed for their severity of disease on the basis of their history of bariatric/ metabolic surgery (whether they had undergone bariatric surgery or not). The patients who had undergone bariatric procedure and their matched controls (both populations positive for Covid-19 infection) were compared to several variables like hospital admission, admission to ICU unit, need for mechanical ventilation & dialysis during hospitalization, other morbidities and also mortality. The comparison of results showed that patients who underwent bariatric surgery had a better prognosis and a better profile (in terms of morbidity and complication rate and severity) as compared to their matched controls indicating an indirect role of bariatric surgery in alleviating the morbidities related with Covid-19 in an obese patient.

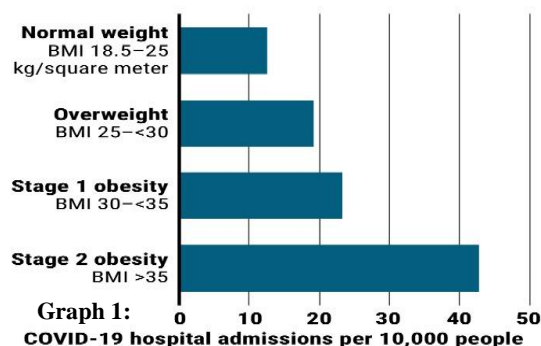
### Introduction:

Bariatric surgery is a modality that aims at 2 kills with one bullet, it ends two of the world's greatest pandemics, obesity and covid-19 altogether.

Obesity has co-morbidities like cardio-metabolic, pulmonary, and thromboembolic diseases; changes in the innate and adaptive immune response; coexistence of a pro-inflammatory state; restrictive changes to the mechanics of the lungs and chest wall; and limited response to mechanical ventilation, this can all lead to poor prognosis of Covid-19 in patients with obesity.

#### The danger of extra kilos

Among 334,000 people in England this spring, the chances of being hospitalized with COVID-19 increased steadily with their body mass index (BMI).



HAMER ET AL., PNAS, 10.1073/PNAS.2011086117

(Graph 1 shows us the relation between increasing obesity and Covid 19 infection severity resulting in increased hospital admissions)

Bariatric surgery offers substantial and sustained weight loss; improvement in obesity-associated pro-inflammatory state, as well as improvement in cardio-metabolic risk factors, including diabetes and blood pressure control; improvement of cardiopulmonary and renal functions; decrease in risk of adverse cardiovascular events; and better survival in patients with severe obesity.

Increased risk for obese patients is also supported by the fact that the coronavirus enters the body via ACE2 receptor (ACE2 is the receptor for SARS-CoV-2). This enzyme is present in cells along the lungs and fat tissue, which yields to the fact that patients with greater weight will have greater viral load. Also, obesity is associated with hyper-inflammation and shortness of breath that makes it difficult to fight the viral infection. This is when bariatric surgery comes into help, after which fat tissue decreases over time in the body, leaving fewer amounts of ACE2 receptors for Covid-19 to access. ACE2 receptors are also present in high amounts in the pericytes of the heart, and brain, thus contributing to the cardiac and CNS effects occurring with Covid-19 infection [1].

The biology of obesity includes impaired immunity (fat cells infiltrate the organs where immune cells are produced and stored, like the spleen, bone marrow, and thymus. Besides, function of T-cells is impaired in the obese state, which also affects production of “memory” T-cells affecting the ability to neutralize future attacks by the same virus.), chronic inflammation, and blood that’s prone to clot, all of which worsen COVID-19.

Another important thing to mention is that obesity leads to higher circulating leptin and lower circulating adiponectin (has anti-inflammatory effect) levels.[2] Adiponectin levels have been reported to be significantly lower in many of the COVID-19 “at risk” groups , therefore bariatric surgery can be useful for indirectly increasing adiponectin which will produce anti-inflammatory effects preventing greater end organ damage.[3,4]

### **Objective:**

To identify bariatric surgery as a modality that reduces Covid-19 related morbidity, mortality and complication rate in the obese patients.

### **Methods:**

#### **Study 1:**

4365 patients were studied in this research study, who were tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between March 8, 2020, and July 22, 2020, in the Cleveland Clinic Health System. 33 patients were identified who had a prior history of bariatric surgery and these patients were matched on a ratio of 1:10 to nonsurgical patients on the basis of the body mass index (BMI) 40.0 or above at the time of SARS-CoV-2 testing. The primary endpoint was the rate of hospital admission. The exploratory endpoints included admission to the intensive care unit (ICU), need for mechanical ventilation and dialysis during hospitalization, and mortality. [5]

#### **Study 2:**

4,248,253 individuals were studied in a retrospective nationwide study with the ages of the patients between 15 to 75 years. The patients chosen in the study were obese and were diagnosed with Covid-19. All obese inpatients, undergoing bariatric surgery or not, were recorded during the hospital stay with a mean observation time of  $5.43 \pm 2.93$  years. This study involved the patients who had undergone bariatric surgery (n=389,671) (including adjustable gastric banding, sleeve gastrectomy, gastric bypass) *versus* who did not undergo bariatric surgery (n=3,858,582) and this variable was compared to different outcomes. The primary outcome was Covid-19 related death and the secondary outcome was the need for invasive mechanical ventilation. [6]

### **Results:**

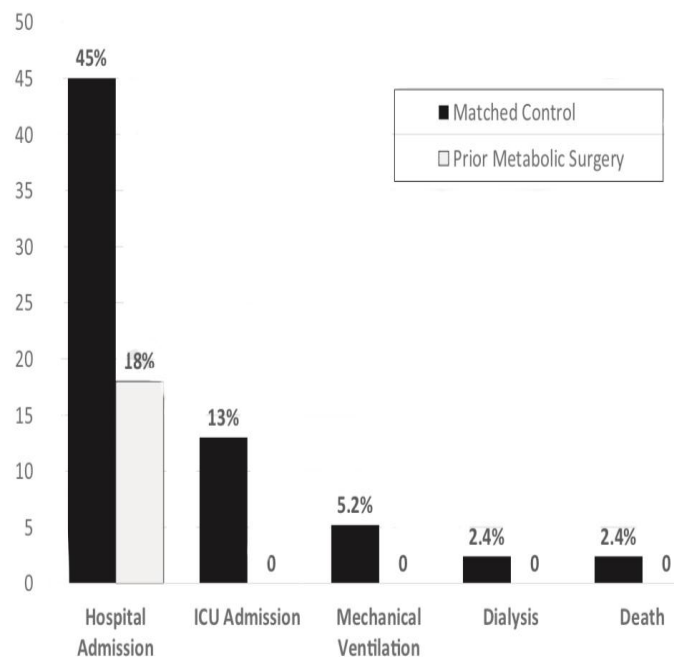
**Study 1:** The average BMI of the surgical group was 49.1 before bariatric surgery and after the procedure it was found to be 37.2 at the time of SARS-CoV-2 testing (compared with the control group’s BMI of 46.7).

Table 1:

Characteristics of metabolic surgery patients and matched control patients at the time of SARS-CoV-2 test

Baseline variable	Metabolic surgery, n = 33	Matched control, n = 330
Sex		
Female	26 (78.8)	239 (78.5)
Male	7 (21.2)	71 (21.5)
Age, years	46.1 ± 12.7	49.8 ± 14.3
BMI, kg/m <sup>2</sup>	37.2 ± 7.1†	46.7 ± 6.4
Race		
White	16 (48.5)	154 (46.7)
Black	13 (39.4)	159 (48.2)
Other	4 (12.1)	17 (5.2)
Ethnicity		
Non-Hispanic	32 (97.0)	319 (96.7)
Hispanic	1 (3.0)	11 (3.3)
Smoking status		
Current	0	1 (.3)
Former	10 (30.3)	100 (30.3)
Never	21 (63.6)	209 (63.6)
Unknown	2 (6.1)	20 (6.1)
Testing location		
Ohio	31 (93.9)	310 (93.9)
Florida	2 (6.1)	20 (6.1)
Hypertension	12 (36.0)‡	205 (62.1)
Diabetes	2 (6.1)§	113 (34.2)
Coronary artery disease	4 (12.0)	22 (6.7)
Heart failure	2 (6.1)	28 (8.5)
Asthma	12 (36.4)	114 (34.5)
COPD	1 (3.0)	10 (3.0)
Cancer	1 (3.0)	10 (3.0)
Steroid	5 (15.0)	56 (17.0)
Angiotensin converting enzyme inhibitor	2 (6.1)	52 (15.8)
Angiotensin receptor blocker	4 (12.0)	35 (10.6)

Table 1: Comparison of several variables between bariatric and non-bariatric patients suffering from covid-19) [5]



Graph 2: Univariate comparison of study outcomes for Covid-19 patients with history of metabolic surgery vs a matched control group with BMI more or equal to 35. (n=330) [5]

In the univariate analysis, 6 (18.2%) patients in the bariatric surgery group and 139 (42.1%) patients in the control group were admitted to the hospital. While none of 4 exploratory outcomes occurred in

the bariatric surgery group, 43 (13.0%) patients in the control group required ICU admission, 22 (6.7%) required mechanical ventilation, 5 (1.5%) required dialysis and 8 (2.4%) died. (Graph 2)

In the multivariate analysis, a prior history of bariatric surgery was associated with a lower hospital admission rate compared with control patients with obesity.

**Study 2:** Out of the 4,248,253 obese patients, 8286 (0.2%) obese individuals were admitted for Covid-19 infection between January 1<sup>st</sup> and May 15<sup>th</sup> 2020.

541 (0.14%) had a history of bariatric surgery and 7,745 (0.2%) did not. Invasive mechanical ventilation was necessary in 14.54% of patients and death occurred in 13.58% of cases. The need for an invasive mechanical ventilation and death occurred in 7% and 3.5% in the bariatric surgery group *versus* 15% and 14.2% in the non-bariatric surgery group, respectively. After a logistic regression, the risk of invasive mechanical ventilation significantly increased with age, being higher in the age class 61-75, male gender, and hypertension, whereas bariatric surgery showed an independent protective effect. Mortality was independently associated with increasing age, male gender, known history of heart failure, cancer, and diabetes, whereas BS was in favor with a protective effect.

Table 2: Univariate analysis of preoperative risk factors distribution in COVID-19 obese patients in BS and NBS cohorts. [6]

Characteristic	No. (%) of Patients		
	Whole population n = 8 286	Bariatric Surgery n = 541	No Bariatric Surgery n = 7 745
Age, mean (SD), y		49.8 (12.0)	59.8 (12.4)
34-45		33 (6.1)	218 (2.8)
15-30		158 (29.2)	899 (11.6)
46-60		239 (44.2)	2231 (28.8)
60-75		111 (20.5)	4397 (56.8)
Gender, M		127 (23.5)	4169 (53.8)
Gender, F		414 (76.5)	3576 (46.2)
COPD, yes		16 (3)	567 (7.3)
COPD, no		525 (97)	7178 (92.7)
Cardiac failure, yes		18 (3.3)	551 (7.1)
Cardiac failure, no		523 (96.7)	7194 (92.9)
Cancer, yes		11 (2)	597 (7.7)
Cancer, no		530 (98)	7148 (92.3)
Diabetes, yes		66 (12.2)	2851 (36.8)
Diabetes, no		475 (87.8)	4894 (63.2)
Hypertension, yes		109 (20.2)	3222 (41.6)
Hypertension, no		432 (78.9)	4523 (58.4)
Invasive mechanical ventilation, yes		38 (7)	1158 (15)
Invasive mechanical ventilation, no		503 (93)	6587 (85)
Death, yes		19 (3.5)	1098 (14.2)
Death, no		522 (96.5)	6647 (85.8)

**Discussion:**

The association between obesity and Covid-19 can be assessed in various aspects. First, obesity causes respiratory system dysfunctions like decreased chest wall elasticity (fat in the abdomen pushes up on the diaphragm, which presses on the lungs and restrict airflow), lung compliance, and expiratory reserve volume (this reduced lung volume causes collapse of airways in the lower lobes of the lungs, where more blood arrives for oxygenation than in the upper lobes). [7]

Second, obesity is associated with disorders such as type 2 diabetes mellitus, atherosclerosis, cardiovascular diseases, hypertension and cancer [8] which are also identified as risk factors for Covid-19. These comorbidities may exacerbate Covid-19 and increase the probability of hospitalization in the intensive care unit (ICU) and also increase mortality [9]. Third, it leads to hyper coagulopathy state and hyper inflammation, and it is well known that venous thromboembolism is a complication of severe Covid-19 infection as well, thus these 2 conditions when present together produce hypercoagulability and thromboembolism in a synergistic way. Inflammatory markers such as IL-6 and C-reactive protein are increased in obese patients [10,11]. These may become so severe that they can cause clots in vital organs and cytokine storm. In all these 3 conditions, the disease is severe and the risk of admission to the ICU and mortality is high. On the other hand, Covid-19 also has an impact on obesity as it increases social constraints and impedes mobility, which thus increases the weight and prevalence of obesity in society, and this gives way to a vicious cycle that is repeated all over again and again.

Although there are ample advantages of bariatric surgery in the Covid-19 patient, there are certain limitations that are worthy of mention. Bariatric surgery, specifically bypass surgery, is likely to have an effect on the absorption of medications that are administered orally to Covid-19 patients.

In case of hydroxychloroquine, a case report of three post-RYGB (Roux-en-Y procedure) patients with autoimmune disease was done (taking standard hydroxychloroquine doses), all three patients had sub therapeutic hydroxychloroquine blood levels and active disease; it was only after increasing their doses above the recommended 400 mg/day dosing that they were able to have therapeutic drug levels as well as better disease control. Thus, hydroxychloroquine has inadequate absorption post-RYGB (and potentially other bariatric procedures), and Covid-19 bariatric patients may need higher doses of hydroxychloroquine than recommended [12].

For azithromycin, a single-dose pharmacokinetic study involving 14 post-gastric bypass patients showed that bioavailability was reduced by 1/3rd in gastric bypass patients, when compared with matched controls [13], since maximal absorption of azithromycin occurs in proximal gut. During RYGB (Roux-en-Y procedure), the stomach is dissected, that leads to less acidic gastric pouch. Azithromycin with its basic nature (alkaline; pKa = 8.5) and low water solubility, the dissolution of the large (500 mg) drug dose of azithromycin can be severely affected post-surgery, thus affecting the absorption and bioavailability of azithromycin. In case of corticosteroids, the pharmacokinetics of dexamethasone and related steroids may be affected, especially post-gastric bypass surgery. These drugs are mainly absorbed via the proximal gut, which is hampered during the bariatric procedure. These are some of the limitations of the bariatric surgery procedure that need to be considered in a covid-19 patient.

**Conclusion:** In the studies that were discussed in this research paper, it made it clear that prior bariatric surgery patients were noted to have weight loss and improvement of metabolic abnormalities, which led to lower rates of morbidity, mortality and hospital & ICU admission in patients with obesity who became infected with SARS-CoV-2 when compared to their matched controls. This helps us in understanding an indirect role of bariatric surgery in alleviating the morbidities related with Covid-19 in an obese patient.

According to the American Society for Metabolic and Bariatric Surgery (ASMBS), the bariatric surgery is not an elective surgery and the lives of patients with obesity is in danger, and it should be acknowledged that a patient who undergoes bariatric surgery is much safer than the Covid-19 patients with obesity [14].



With limited research material available globally on the relation between bariatric surgery and Covid-19, there is much more research required in this field and more cues to be solved. Bariatric surgery can be a promising modality for reducing the severity of Covid-19 in obese patients with further advances in the near future.

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