Effects of Bariatric Surgery on COVID-19: a Multicentric Study from a High Incidence Area

Federico Marchesi1,2 · Marina Valente1 · Matteo Riccò3 · Matteo Rottoli4,5 · Edoardo Baldini6 · Fouzia Mecheri7 · Stefano Bonilauri8 · Sergio Boschi9 · Paolo Bernante4,5 · Andrea Sciannamea4 · Jessica Rolla10 · Alice Francescato7 · Ruggero Bollino8 · Concetto Cartelli8 · Andrea Lana8 · Francesca Anzolin11 · Paolo Del Rio1 · Diletta Fabbì12 · Gabriele Luciano Petracca1 · Francesco Tartamella1 · Giorgio Dalmonte1

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Abstract

Introduction The favorable effects of bariatric surgery (BS) on overall pulmonary function and obesity-related comorbidities could influence SARS-CoV-2 clinical expression. This has been investigated comparing COVID-19 incidence and clinical course between a cohort of patients submitted to BS and a cohort of candidates for BS during the spring outbreak in Italy.

Materials and Methods From April to August 2020, 594 patients from 6 major bariatric centers in Emilia-Romagna were administered an 87-item telephonic questionnaire. Demographics, COVID-19 incidence, suggestive symptoms, and clinical outcome parameters of operated patients and candidates to BS were compared. The incidence of symptomatic COVID-19 was assessed including the clinical definition of probable case, according to World Health Organization criteria.

Results Three hundred fifty-three operated patients (Op) and 169 candidates for BS (C) were finally included in the statistical analysis. While COVID-19 incidence confirmed by laboratory tests was similar in the two groups (5.7% vs 5.9%), lower incidence of most of COVID-19-related symptoms, such as anosmia (p: 0.046), dysgeusia (p: 0.049), fever with rapid onset (p: 0.046) were recorded among Op patients, resulting in a lower rate of probable cases (14.4% vs 23.7%; p: 0.009). Hospitalization was more frequent in C patients (2.4% vs 0.3%, p: 0.02). One death in each group was reported (0.3% vs 0.6%). Previous pneumonia and malignancies resulted to be associated with symptomatic COVID-19 at univariate and multivariate analysis.

Conclusion Patients submitted to BS seem to develop less severe SARS-CoV-2 infection than subjects suffering from obesity.

Keywords Obesity · COVID-19 · SARS-CoV-2 · Bariatric surgery
Introduction

The role of bariatric surgery (BS) in weight reduction is undisputed [1]. Surgery in patients suffering from severe obesity leads to successful long-term weight loss and improvement of the main obesity-related comorbidities, such as diabetes, hypertension, obstructive sleep apnea, and hyperlipidemia [2–4]. Furthermore, surgically induced weight loss markedly improves the overall pulmonary function in patients with obesity [5], leading to significant reduction in both respiratory impairment and systemic inflammation related to obesity [6].

In the light of the above, a protective role of BS versus respiratory infectious disease is conceivable. Indeed, during the 2009 influenza pandemic, obesity was recognized as an independent risk factor for severe H1N1 pulmonary infection [7] as well as for the development of influenza-related systemic complications [8].

In December 2019, a new coronavirus causing a severe acute respiratory syndrome emerged in Wuhan, China [9]. The novel coronavirus 2 (SARS-CoV-2) and subsequent SARS-CoV-2-induced coronavirus disease 2019 (COVID-19) spread very rapidly worldwide and were classified as a pandemic by the World Health Organization (WHO) on March 11, 2020.

Between late February and April, Italy faced a massive outbreak of COVID-19, with more than 200,000 confirmed infected patients by the end of April. Furthermore, northern Italy had one of the highest clinical burdens in the world, with data showing a tremendously high case fatality rate (CFR), up to 15–18% in high incidence areas [10]. The clinical manifestations of COVID-19 run from asymptomatic disease to severe acute respiratory infection requiring hospitalization, with oxygen support or intensive care and invasive ventilation [11]. Old age and the presence of comorbidities have been reported as risk factors for more severe disease and death [12]. The pathways that underlie inter-individual variability and that can thus be predictors of worse clinical presentation are not yet fully clear.

It is plausible that severe obesity, per se and due to its associated comorbidities, may impact on the clinical course of infected patients.

The aim of this study was to assess whether BS may influence the clinical course of COVID-19 by investigating possible discrepancies in clinical presentation and outcomes between patients undergone BS and a cohort of patients with obesity candidates for BS, particularly in the exceptional scenario of the epidemic that overburdened Northern Italy National Healthcare System.

Methods

Study Design and Setting

This is a multicentric retrospective observational cross-sectional study, involving 6 major centers of bariatric surgery in Emilia Romagna, Northern Italy. Clinical data regarding patients that had already undergone a bariatric procedure were compared with those of patients waiting for BS in the above-mentioned hospitals. Inclusion criteria were age above 18 years and ability to give a valid informed consent. We excluded from the analysis (a) subjects who resided outside the Emilia Romagna, Lombardy, Veneto, Liguria and Marche regions from February 24 and August 31, 2020; (b) subjects that underwent a bariatric procedure other than adjustable gastric band (AGB), sleeve gastrectomy (SG), Roux-en-Y Gastric By-pass (RYGB), and One Anastomosis Gastric By-pass (OAGB); and (c) subjects that had undergone the intervention less than 12 months before the interview. The subjects were enrolled from June to August 2020.

All the subjects had been interviewed by phone by medical members of the bariatric teams. If a patient was unable to answer the survey (e.g., death), information was gathered from relatives. Data regarding hospital diagnosis, admission, and outcomes were confirmed consulting hospital registries.

Ethics and Consent Form

Ethical approvals of the study protocol were obtained by each center from the relevant Ethics Committee and informed consent obtained from all subjects. All data were handled and stored in accordance with the European Union General Data Protection Regulation (EU GDPR) 2016/679 [13].

Data Collection and Variables

All patients defined as eligible to undergo bariatric surgery met the 2020 EAES Clinical Practice Guidelines on bariatric surgery [14]. The bariatric procedures considered (AGB, SG, RYGB, and OAGB) account for 96.8% of all bariatric procedures performed worldwide, being also representative of the Italian recent trend in BS [15]. Patients submitted to procedures for which the study center had no certified expertise (at least 10 procedures) were not included. Among operated patients, only subjects that had undergone the procedure more than 12 months before the interview were considered for the analysis. This is normally the minimum time to weight loss stabilization and remission of comorbidities [16, 17].

Each patient was administered a questionnaire consisting of 87 questions, mostly closed-ended, divided into 11 sections including geographic data, demographic data, bariatric surgery history, comorbidities, vaccination history, clinical evaluation, diagnostic assessment, and outcome parameters.

Demographic variables included anthropometric characteristics. COPD, obstructive sleep apnea syndrome (OSAS), hypertension, diabetes, the use of insulin, hypertriglyceridemia, hypercholesterolemia, smoking habit, concomitant pneumonia, autoimmune diseases, immunodeficiencies, and
malignancies were considered as comorbidities able to influence the clinical course.

Chronic use of ACE inhibitors, hydroxychloroquine, or steroids was also recorded for its supposed relation with COVID-19 [18–20]. Vaccination history (seasonal influenza, pneumococcus, BCG) was collected as well, because of the supposed role of vaccinations in mitigating the infection severity [21–24].

In the clinical evaluation section, the following symptoms reported from February 24 were considered: fever (>37.5 °C), fever at rapid onset, shivering, cough, productive cough, anosmia, ageusia, asthenia, myalgia, headache, sore throat, running nose, nausea or vomit, diarrhea, and conjunctivitis.

In the diagnostic section, we recorded nasopharyngeal swabs, serologic tests, chest x-rays, or chest CT scans. Any hospital admission, length of hospital stay, need of oxygen supplemental therapy, non-invasive ventilation (NIV), ICU admission, and death were considered as indicators of the severity of COVID-19.

In agreement with the latest definitions given by the WHO, patients with a laboratory confirmation (nasopharyngeal swab or serologic test) for SARS-CoV-2 were considered as confirmed COVID-19 cases (CC). During the epidemic peak, the shortage of diagnostic tools led to a high rate of undiagnosed patients [25]; therefore, we mainly focused on the group of probable COVID-19 cases (PC), including, in addition to CC patients, subjects meeting the WHO clinical criteria for “probable cases.” Specifically, we included patients residing in regions considered as very high risk of transmission who had experienced since February 24, 2020, an episode of anosmia/dysgeusia or had a chest imaging suggestive of COVID-19 or the association of rapid onset fever (self-measured temperature ≥37.5 °C) and cough or the association of any three or more of the following signs and symptoms: fever, cough, general weakness, headache, myalgia, sore throat, nose discharge/swelling, nausea/vomiting, or diarrhea [26].

For the above reasons, patients residing in medium or low incidence regions were excluded.

Factors influencing the incidence of symptomatic forms (PC) and outcome parameters (hospitalization) were investigated through univariate and multivariate analysis.

**Statistical Analysis**

Continuous variables were described as mean ± standard deviation. Categorical variables were considered in a numerical manner and as holding percentages. At the beginning, continuous variables were analyzed with D’Agostino-Pearson test, in order to verify distribution, assuming normal distribution as the one identified by a corresponding p value > 0.100.

Continuous variables were compared with Student’s t test in the case of normal distribution, or with Mann-Whitney, if normal distribution was rejected. The distribution of dichotomous variables related to the outcomes “probable case” vs “non-probable case”; “COVID-19 positive” vs “COVID-19 negative”; “hospitalization” vs “non-hospitalization” was initially assessed by means of chi-squared test, estimating the corresponding p value. All variables associated with a p value < 0.2 were included in a model of multivariate analysis through binary logistic regression, estimating corresponding odds ratio (OR) values with their 95% confidence interval (CI95%).

Assuming a point prevalence of 2.8% for SARS-CoV-2 IgG positivity [27], a probability of falsely rejecting a true null hypothesis (α) = 0.05, with Zα = 1.96 a minimum sample size of 42 participants from every center, (i.e., minimum sample size of 210 participants) was calculated.

**Results**

Out of the 594 patients interviewed, 25 were excluded due to epidemiological criteria and 47 were excluded because they met other exclusion criteria.

353 patients operated (Op) and 169 candidates for BS (C) were finally included in the statistical analysis. Sleeve gastrectomy (SG) was the most common procedure performed (65.2%), followed by Roux-en-Y gastric bypass (RYGB) (31.6%), adjustable gastric banding (AGB) (2.3%) and One Anastomosis gastric bypass (OAGB) (1.1%), reflecting the Italian proportion according to SICOB (Italian society of obesity surgery) registry [28]. Op and C groups were similar for mean age and sex proportion (Table 1).

As predictable effect for BS, Op patients presented a significant lower BMI (30.7 vs 43.5, p<0.001) and lower incidence of main comorbidities, such as obstructive sleep apnea syndrome, hypertension, diabetes, hypertriglyceridemia and hypercholesterolemia (Table 2). No significant difference was found in smoking habits, previous pulmonary, autoimmune or neoplastic disease or immunodeficiency.

Vaccination history and chronic use of hydroxychloroquine or steroids was similar in the two groups too (Table 2).

The use of ACE inhibitors was lower in Op group, probably owing to hypertension improvement.

Among Op patients, we recorded a lower incidence of most COVID-19-related symptoms (Table 3), such as anosmia (p:0.046), ageusia/dysgeusia (p: 0.049), fever with rapid onset (p: 0.046), asthenia (p: 0.034), and particularly cough (p: 0.001) and productive cough (p: 0.009).

Probably as result of the above, a higher percentage of C patients was submitted to nasal swab (24.3 vs 11.6, p: 0.001) (Table 3).

The rate of probable cases was respectively 14.4% in Op patients and 23.7% in the C group, with a statistically significant difference (p: 0.009). We recorded a significantly
different distribution of PC among the provinces of Emilia Romagna region, with a decreasing rate going from northwest to southeast (41.6% in Piacenza, 4.6% in Bologna).

Considering only CC, incidence was respectively 5.7% in Op patients and 5.9% in the C group (p:0.908) (Table 3).

Hospitalization was more frequent in C patients (2.4% vs 0.3%, p: 0.02) as well as O2 therapy (2.4% vs 0.3%, p:0.02). No patient was admitted to the ICU. We had 1 death in Op patients (0.3%) and 1 in the C group (0.6%) (Table 3).

Univariate analysis indicated OSAS, hypertension, diabetes, pneumonia, autoimmune diseases, previous nonbariatric surgery, malignancy, the use of ACE-inhibitors as related to COVID-19 probable infection (Table 4). Surprisingly, 2019–2020 seasonal flu vaccination was associated with probable SARS-CoV-2 infection (i.e. 31.9% in probably infected patients vs 20.9% in probably not infected patients; p: 0.03). Considering only CC, solely autoimmune diseases showed a significant correlation (p: 0.007) (Table 5), confirmed also by the multivariate analysis.

Interestingly, the type of bariatric procedure seems also to correlate with COVID-19 probable infection, with a relatively higher frequency of RYGB among PC (Table 4).

Diabetes, hypertension, and the use of ACE-inhibitors resulted as predictive of hospital admission (Table 6).

At multivariate analysis, only previous pneumonia and malignancies confirmed to be associated with PC (OR: 3.536, 95%CI: 1.961; 7.040, and OR: 2.786, 95%CI: 1.255; 7.022, respectively) (Table 7), while hypertension, diabetes, and the use of ACE inhibitors did not confirm to be associated with hospital admission (Table 7).

### Discussion

The outbreak of the SARS-Cov-2 pandemic laid bare structural deficiency in healthcare systems along with individual frailties all over the world. Besides old age, the death toll of this “tsunami” has shown to be proportional to pulmonary and metabolic comorbidities and to the availability of dedicated healthcare facilities, especially at the peak of the epidemic curve [29]. From this point of view, patients suffering from obesity certainly represent a paradigmatic target.

From February 24, 2020 Italy experienced a rapid spread of COVID-19 becoming, on March 9, 2020, the country with the second highest total number of COVID-19 cases [30]. According to the Italian National Institute of Health (ISS), by May 4 in Italy, there were 209,254 cases of COVID-19 and 26,892 associated deaths (https://www.epicentro.iss.it/en/coronavirus/bollettino/Infografica_4maggio_ENG.pdf). Geographical spread was heterogeneous: at its highest in the Northern regions and at its lowest in the Southern regions and in the main Islands [31, 32]. As a consequence, 91% of the excess mortality recorded in March 2020 was concentrated in the Northern Italy regions and in the Marche central Italy region. Due to this peculiar epidemic distribution, the Italian

### Table 1 Demographics

|                      | Total N=522 | Op N = 353 | C N = 169 | P value |
|----------------------|-------------|------------|-----------|---------|
| Age (years; average ± SD) | 47.8 ± 11.0 | 48.3 ± 11.2 | 46.5 ± 10.5 | 0.074 |
| Age stratification (N; %) |             |            |           | 0.226 |
| < 30 years           | 37          | 7.1        | 23        | 6.5     | 14 | 8.3 |
| 30–39 years          | 83          | 15.9       | 56        | 15.9    | 27 | 16.0 |
| 40–49 years          | 149         | 28.5       | 97        | 27.5    | 52 | 30.8 |
| 50–59 years          | 188         | 36.0       | 124       | 35.1    | 64 | 37.9 |
| 60–69 years          | 59          | 11.3       | 48        | 13.6    | 11 | 6.5 |
| ≥ 70 years           | 6           | 1.1        | 5         | 1.4     | 1  | 0.6 |
| Sex (male) (N; %)    | 117         | 22.4       | 71        | 20.1    | 46 | 27.2 | 0.069 |
| Weight (kg; mean ± SD) | 95.1 ± 26.7 | 83.4 ± 18.2 | 119.6 ± 25.0 | < 0.001 |
| Height (cm; mean ± SD) | 164.9 ± 9.1 | 164.5 ± 8.9 | 165.5 ± 9.3 | 0.241 |
| BMI (kg/m²; mean ± SD) | 34.9 ± 8.8 | 30.7 ± 5.7 | 43.5 ± 7.8 | < 0.001 |
| Type of surgery (N; %) |             |            |           |         |
| AGB                  | 8           | 1.5        | 8         | 2.3     | –  | –   |
| RYGB                 | 111         | 21.3       | 111       | 31.6    | –  | –   |
| SG                   | 230         | 44.1       | 230       | 65.2    | –  | –   |
| OAGB                 | 4           | 0.8        | 4         | 1.1     | –  | –   |
| Waiting list         | 169         | 32.4       | –         |         | 169 | 100 |

Op Operated patients; C Candidates for surgery; BMI Body Mass Index; AGB Adjustable Gastric Banding; RYGB Roux-en-Y Gastric Bypass; SG Sleeve Gastrectomy; OAGB One Anastomosis Gastric Bypass
Government deployed several preventive measures to curb the spread of the syndrome, banning travels between regions from the beginning of the pandemic, and finally with a lockdown of the entire territory on March 11, 2020. The specific demographic structure (old age and comorbidities) has been put forward, among other factors, to justify the stunning Italian CFR compared, for example, with the Chinese trend. Nevertheless, during the epidemic peak, due to the shortage of diagnostic tools, SARS-CoV-2 infection prevalence was most likely underestimated, affecting the reliability of many parameters, such as CFR. Indeed, only severely symptomatic patients were tested during the peak and the real proportion of mild symptomatic or asymptomatic population was not deeply investigated. In fact, only one study conducted in a small area of the north east [33] screened the entire population, revealing a rate of 41.1% of asymptomatic confirmed SARS-CoV-2 infections at the beginning of the outbreak.

Any attempt to assess a reliable incidence rate during the outbreak peak was therefore inconclusive. For these reasons, the “clinical” prevalence of COVID-19 (i.e., clinical manifestations, hospitalization, deaths) rather than its tested prevalence has been taken into account in this study.

According to the Italian Obesity Barometer Report 2019 [34], over 1 out of 3 Italians is overweight, and, more notably, 1 out of 10 suffers from obesity. It goes without saying that obesity, per se and due to its comorbidities, has been considered as a risk factor for increased susceptibility to infections and sepsis-related mortality [35]. In this regard, a predisposing role of obesity towards severe clinical course of COVID-19 could be reasonably assumed.

In our series, we recorded a significantly lower incidence of COVID-19 symptoms among patients who had previously undergone a bariatric procedure for severe obesity. Some of the collected symptoms are typical of pathogenetic human coronaviruses, with fever and cough reported most commonly [36], while others (anosmia and dysgeusia) have been recently reported as pathognomonic of SARS-CoV-2 infection [37].

Table 2  Comorbidities, therapy, and vaccinations

| Comorbidities                  | Total N = 522 | Op N = 353 | C N = 169 | P value |
|-------------------------------|---------------|------------|-----------|---------|
| N %                           | N %           | N %        | N %       |         |
| COPD                          | 35 6.7        | 21 5.9     | 14 8.3    | 0.318   |
| OSAS                          | 105 20.1      | 57 16.1    | 48 28.4   | 0.001   |
| B-PAP/C-PAP                   | 35 6.7        | 23 6.5     | 12 7.1    | 0.803   |
| Hypertension                  | 166 31.8      | 97 27.5    | 69 40.8   | 0.002   |
| Diabetes/oral hypoglycemic    | 62 11.9       | 34 9.6     | 28 16.6   | 0.022   |
| Diabetes/insulin              | 11 2.1        | 1 0.3      | 10 5.9    | <0.001  |
| Hypertriglyceridemia          | 64 12.3       | 32 9.1     | 32 18.9   | 0.001   |
| Hypercholesterolemia          | 127 24.3      | 71 20.1    | 56 33.1   | 0.001   |
| Smoking                       | 147 28.2      | 96 27.2    | 51 30.2   | 0.478   |
| Surgery (non-bariatric)       | 376 72.0      | 243 68.8   | 133 78.7  | 0.019   |
| Previous pneumonia            | 57 10.9       | 34 9.6     | 23 13.6   | 0.173   |
| Autoimmune diseases           | 39 7.5        | 23 6.5     | 16 9.5    | 0.230   |
| Malignancies                  | 30 5.7        | 20 5.7     | 10 5.9    | 0.908   |
| Immune deficiencies           | 15 2.9        | 9 2.5      | 6 3.6     | 0.522   |
| **Therapy**                   |               |            |           |         |
| ACE-inhibitors                | 75 14.4       | 44 12.5    | 31 18.3   | 0.073   |
| Colchicine                    | 2 0.4         | 1 0.3      | 1 0.6     | 0.594   |
| Hydroxychloroquine            | 2 0.4         | 1 0.3      | 1 0.6     | 0.594   |
| Steroids                      | 19 3.6        | 14 4.0     | 5 3.0     | 0.565   |
| **Vaccine**                   |               |            |           |         |
| Seasonal Flu, 2019–2020       | 119 22.8      | 77 21.8    | 42 24.9   | 0.439   |
| Seasonal Flu, any             | 170 32.6      | 116 32.9   | 54 32.0   | 0.836   |
| BCG                           | 78 14.9       | 57 16.1    | 21 12.4   | 0.264   |
| Pneumonia, any                | 44 8.4        | 28 7.9     | 16 9.5    | 0.555   |

Op Operated patients; C Candidates for surgery; COPD Chronic Obstructive Pulmonary Disease; OSAS Obstructive Sleep Apnea Syndrome; BCG Bacillus Calmette–Guérin.
symptoms specificity and assessing a more reliable parameter of symptomatic COVID-19 incidence. Based on PC rates, we can state that Op patients are less predisposed to symptomatic COVID-19 (14.4% vs 23.7% p:0.009); on the other hand, we can suppose that SARS-CoV-2 real incidence in the population of the study was probably higher than the one estimated based on the regional data during the outbreak [27, 33, 38].

It is not reasonable to ascribe this trend to a different rate of infection among Op, C patients and normal population, there being no evident social or behavioral difference able to modify the exposure to the virus. Conversely, as for other infections, it is more likely that obesity could mainly promote the clinical expression of the virus. In fact, the literature gives clear evidence that one of the typical features of severe obesity

| Symptoms | Total N = 522 | Op N = 353 | C N = 169 | P value |
|----------|--------------|------------|-----------|---------|
| Any      | 161 (30.8%)  | 93 (26.3%) | 68 (40.2%)| 0.001   |
| Fever (> 37.5 °C) | 65 (12.5%)  | 38 (10.7%) | 27 (16.0%)| 0.092   |
| Fever rapid onset | 41 (7.9%)    | 22 (6.2%)  | 19 (11.2%)| 0.046   |
| Shivering | 44 (8.4%)    | 24 (6.8%)  | 20 (11.8%)| 0.053   |
| Cough    | 39 (7.5%)    | 17 (4.8%)  | 22 (13.0%)| 0.001   |
| Productive cough | 16 (3.1%)    | 6 (1.7%)   | 10 (5.9%) | 0.009   |
| Anosmia  | 21 (4.0%)    | 10 (2.8%)  | 11 (6.5%) | 0.046   |
| Ageusia/dysgeusia | 26 (5.0%)   | 13 (3.7%)  | 13 (7.7%) | 0.049   |
| Asthenia | 53 (10.2%)   | 29 (8.2%)  | 24 (14.2%)| 0.034   |
| Myalgia  | 60 (11.5%)   | 37 (10.5%) | 23 (13.6%)| 0.294   |
| Headache | 65 (12.5%)   | 38 (10.8%) | 27 (16.0%)| 0.092   |
| Sore throat | 47 (9.0%)   | 28 (7.9%)  | 19 (11.2%)| 0.216   |
| Running nose | 55 (10.5%)  | 31 (8.8%)  | 24 (14.2%)| 0.059   |
| Nausea/Vomiting | 26 (5.0%)   | 14 (4.0%)  | 12 (7.1%) | 0.123   |
| Diarrhea | 34 (6.5%)    | 23 (6.5%)  | 11 (6.5%) | 0.998   |
| Conjunctivitis | 16 (3.1%)   | 10 (2.8%)  | 6 (3.6%)  | 0.656   |

| Length of fever (days; average ± SD) | 6.8 ± 8.8 | 6.6 ± 8.4 | 7.2 ± 9.7 | 0.800 |
| Length of symptoms (days; average ± SD) | 8.8 ± 11.7 | 7.9 ± 8.7 | 9.8 ± 14.7 | 0.399 |

| Diagnosis | Total N = 522 | Op N = 353 | C N = 169 | P value |
|-----------|--------------|------------|-----------|---------|
| Nasal swab | 82 (15.7%)  | 41 (11.6%) | 41 (24.3%)| <0.001 |
| Of them, positive | 13 (15.9%) | 6 (14.6%) | 7 (17.1%) | 0.762 |
| Serological tests | 55 (10.5%) | 36 (10.2%) | 19 (11.2%)| 0.716 |
| Of them, positive | 25 (45.5%) | 18 (50.0%) | 7 (36.8%) | 0.351 |
| Chest X-rays | 17 (3.3%)   | 8 (2.3%)   | 9 (5.3%)  | 0.065 |
| Of them, positive | 5 (29.4%)  | 2 (25.0%)  | 3 (33.3%) | 0.707 |
| Chest CT Scan | 8 (1.5%)    | 6 (1.7%)   | 2 (1.2%)  | 0.653 |
| Of them, positive | 2 (25.0%)  | 1 (16.7%)  | 1 (50.0%) | 0.346 |

| Confirmed cases | Total N = 522 | Op N = 353 | C N = 169 | P value |
|-----------------|--------------|------------|-----------|---------|
| Hospital admission | 5 (1)      | 1 (0.3%)   | 4 (2.4%)  | 0.022  |
| O2 therapy      | 5 (1)       | 1 (0.3%)   | 4 (2.4%)  | 0.022  |
| NIV             | 1 (0.2%)    | 0 –        | 1 (0.6%)  | 0.148  |
| ICU             | 0 –         | 0 –        | 0 –       | –      |
| Death           | 2 (0.4%)    | 1 (0.3%)   | 1 (0.6%)  | 0.581  |
| Hospital stay (days; average ± SD) | 15.2 ± 21.5 | 4.0       | 17.4 ± 23.3 | 0.672 |

Op: Operated patients; C: Candidates for surgery; CT: Computed Tomography; ICU: Intensive Care Unit; NIV: Non-Invasive Ventilation

Table 3 Covid-19 related symptoms, tests, and outcomes
is persistent hyperleptinemia produced by a state of leptin resistance. Leptin has been recognized as a key link between nutritional status and immune response, and it is an important mediator of pulmonary immunity [39, 40]. Furthermore, adipose tissue inflammation is a hallmark of obesity: macrophage accumulation in adipose tissue provides a mechanism for adipocyte production of the proinflammatory cytokines, thus leading to chronic low-grade inflammation, which may impair immune response and have detrimental effects on the lung parenchyma and bronchi [41]. Substantiating this, the Centers for Disease Control and Prevention considers patients with BMI ≥ 40 kg/m² at risk for flu complications [42–44].

| Table 4  | Univariate analysis: characteristics by status (COVID-19 probable vs. not probable) |
| --- | --- |
| Total N=522 | Probable N = 91 | Not probable N = 431 | P value |
| ≥ 60 years | N | % | N | % | N | % |  |
| 253 | 48.5 | 51 | 56.0 | 202 | 46.9 | 0.111 |
| Sex (male) | N | % | N | % | N | % |  |
| 117 | 22.4 | 21 | 23.1 | 96 | 22.3 | 0.867 |
| BMI ≥ 30 kg/m² | N | % | N | % | N | % |  |
| 341 | 65.3 | 63 | 69.2 | 278 | 64.5 | 0.389 |
| BMI ≥ 35 kg/m² | N | % | N | % | N | % |  |
| 234 | 44.8 | 48 | 52.7 | 186 | 42.2 | 0.095 |
| Type of surgery |  |
| AGB | N | % | N | % | N | % |  |
| 8 | 1.5 | 1 | 1.1 | 7 | 1.6 | 0.012 |
| RYGB | 111 | 21.3 | 24 | 26.4 | 87 | 20.2 |
| SG | 230 | 44.1 | 26 | 28.6 | 204 | 47.3 |
| OAGB | 4 | 0.8 | 0 | 0 | 4 | 0.9 |
| Waiting list | 169 | 32.4 | 40 | 44 | 129 | 29.9 |
| Comorbidities |  |
| COPD | 35 | 6.7 | 8 | 8.8 | 27 | 6.3 | 0.381 |
| OSAS | 105 | 20.1 | 30 | 33.0 | 75 | 17.4 | 0.001 |
| B-PAP/C-PAP | 35 | 6.7 | 9 | 9.9 | 26 | 6.0 | 0.269 |
| Hypertension | 166 | 31.8 | 45 | 49.5 | 121 | 28.1 | <0.001 |
| Diabetes (any) | 65 | 12.5 | 18 | 19.8 | 47 | 10.9 | 0.020 |
| Diabetes/Oral hypoglycemic | 62 | 11.9 | 17 | 18.7 | 45 | 10.4 | 0.027 |
| Diabetes/ Insulin | 11 | 2.1 | 2 | 2.2 | 9 | 2.1 | 0.947 |
| Hypertriglyceridemia | 64 | 12.3 | 16 | 17.6 | 48 | 11.1 | 0.088 |
| Hypercholesterolemia | 127 | 24.3 | 29 | 31.9 | 98 | 22.7 | 0.065 |
| Smoking | 147 | 28.2 | 30 | 33.0 | 117 | 27.1 | 0.262 |
| Surgery (non-bariatric) | 376 | 72 | 74 | 81.3 | 302 | 70.1 | 0.030 |
| Previous pneumonia | 57 | 10.9 | 22 | 24.2 | 35 | 8.1 | <0.001 |
| Autoimmune diseases | 39 | 7.5 | 12 | 13.2 | 27 | 6.3 | 0.022 |
| Malignancies | 30 | 5.7 | 11 | 12.1 | 19 | 4.4 | 0.004 |
| Immune deficiencies | 15 | 2.9 | 3 | 3.3 | 12 | 2.8 | 0.790 |
| Therapy |  |
| ACE-inhibitors | 75 | 14.4 | 25 | 27.5 | 50 | 11.6 | <0.001 |
| Colchicine | 2 | 0.4 | 0 | – | 2 | 0.5 | 0.515 |
| Hydroxychloroquine | 2 | 0.4 | 0 | – | 2 | 0.5 | 0.515 |
| Steroids | 19 | 3.6 | 4 | 4.4 | 15 | 3.5 | 0.672 |
| Vaccine |  |
| Seasonal Flu, 2019–2020 | 119 | 22.8 | 29 | 31.9 | 90 | 20.9 | 0.023 |
| Seasonal Flu, any | 170 | 32.6 | 36 | 39.6 | 134 | 31.1 | 0.117 |
| BCG | 78 | 14.9 | 17 | 18.7 | 61 | 14.2 | 0.271 |
| Pneumonia, any | 44 | 8.4 | 10 | 11.0 | 34 | 7.9 | 0.333 |

BMI Body Mass Index; AGB Adjustable Gastric Banding; RYGB Roux-en-Y Gastric Bypass; SG Sleeve Gastrectomy; OAGB One Anastomosis
Gastric Bypass; COPD Chronic Obstructive Pulmonary Disease; OSAS Obstructive Sleep Apnea Syndrome; BCG Bacillus Calmette–Guérin
Moving to the outcome parameters, we did report a statistically significant difference in the rates of hospitalization (0.3% vs 2.4%, \( p: 0.02 \)) as well as in the rate of \( O_2 \) therapy \( (p: 0,02) \) among the Op and C groups. Severe obesity is in fact associated with impairment of total respiratory system compliance, leading to reduced functional residual capacity and decreased expiratory reserve volume \([45, 46]\), which can be responsible for difficult ventilation and the need of oxygen support in these patients. In fact, it is undisputed that respiratory impairment was the main criteria for hospital and ICU admission (no cases in our series). The low number of deaths in our study does not allow any definitive conclusion to be drawn about the role of BS in reducing COVID-19 mortality: studies on larger population should assess whether, as expected, the outcome trend will be confirmed.

OSAS, hypertension, diabetes, previous pneumonia, autoimmune diseases, malignancies, and the use of ACE-inhibitors were found as predictive of SARS-CoV-2 probable infection at univariate analysis, whereas at multivariate analysis only previous pneumonia and malignancies were confirmed.

Our data are in line with the results of a recent meta-analysis on more than 75,000 patients, in which hypertension, cardiovascular disease, diabetes, and malignancies were the most prevalent pre-existing comorbidities in hospitalized patients for COVID-19 \([29]\). Moreover, a recent study \([47]\) has

| Table 5 Univariate analysis: characteristics by status (Covid-19 positive vs. negative) |
|-----------------------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                              | Total \( N = 522 \) | Positive \( N = 30 \) | Negative \( N = 492 \) | P value |
|                                              | N | % | N | % | N | % |
| ≥ 60 years                                   | 253 | 48.5 | 17 | 56.7 | 236 | 48.0 | 0.355 |
| Sex (male)                                   | 117 | 22.4 | 6 | 20.0 | 111 | 22.6 | 0.744 |
| BMI ≥ 30 kg/m2                                | 341 | 65.3 | 16 | 53.3 | 325 | 66.1 | 0.155 |
| BMI ≥ 35 kg/m2                                | 234 | 44.8 | 10 | 33.3 | 224 | 45.5 | 0.192 |
| Comorbidities                                |                         |                 |                         |                 |
| COPD                                         | 35 | 6.7 | 2 | 6.7 | 33 | 6.7 | 0.993 |
| OSAS                                         | 105 | 20.1 | 3 | 10.0 | 102 | 20.7 | 0.155 |
| B-PAP/C-PAP                                  | 35 | 6.7 | 1 | 3.3 | 34 | 6.9 | 0.447 |
| Hypertension (any)                           | 166 | 31.8 | 11 | 36.7 | 155 | 31.5 | 0.556 |
| Diabetes (oral hypoglycemic)                 | 62 | 11.9 | 5 | 16.7 | 57 | 11.6 | 0.404 |
| Diabetes/Insulin                             | 11 | 2.1 | 0 | – | 11 | 2.2 | 0.408 |
| Hypertriglyceridemia                         | 64 | 12.3 | 6 | 20.0 | 58 | 11.8 | 0.183 |
| Hypercholesterolemia                         | 127 | 24.3 | 11 | 36.7 | 116 | 23.6 | 0.105 |
| Smoking                                      | 147 | 28.2 | 8 | 26.7 | 139 | 28.3 | 0.851 |
| Surgery (non-bariatric)                      | 376 | 72.0 | 25 | 83.3 | 351 | 71.3 | 0.155 |
| Previous pneumonia                           | 57 | 10.9 | 6 | 20.0 | 51 | 10.4 | 0.100 |
| Autoimmune diseases                          | 39 | 7.5 | 6 | 20.0 | 33 | 6.7 | 0.007 |
| Malignancies                                 | 30 | 5.7 | 1 | 3.3 | 29 | 5.9 | 0.558 |
| Immune deficiencies                          | 15 | 2.9 | 1 | 3.3 | 14 | 2.8 | 0.877 |
| Therapy                                      |                         |                 |                         |                 |
| ACE-inhibitors                               | 75 | 14.4 | 7 | 23.3 | 68 | 13.8 | 0.149 |
| Hydroxychloroquine                           | 2 | 0.4 | 0 | – | 2 | 0.5 | 0.726 |
| Steroids                                     | 19 | 3.6 | 2 | 6.7 | 17 | 3.5 | 0.362 |
| Vaccine                                      |                         |                 |                         |                 |
| Seasonal Flu, 2019–2020                       | 119 | 22.8 | 6 | 20.0 | 113 | 23.0 | 0.707 |
| Seasonal Flu, any                            | 170 | 32.6 | 6 | 20.0 | 164 | 33.3 | 0.130 |
| BCG                                          | 78 | 14.9 | 7 | 23.3 | 71 | 14.4 | 0.184 |
| Pneumonia, any                               | 44 | 8.4 | 3 | 10.0 | 41 | 8.3 | 0.750 |

BMI Body Mass Index; COPD Chronic Obstructive Pulmonary Disease; OSAS Obstructive Sleep Apnea Syndrome; BCG Bacillus Calmette–Guérin
found an association of type 2 diabetes with COVID-19 likely event in a cohort of patients undergone BS at 12 months follow-up.

Reducing the analysis to confirmed positive cases only, autoimmune diseases alone showed a significant positive correlation, both in univariate and multivariate analysis. However to date, available records in the literature are still not conclusive on this aspect [48, 49].

Along with BMI, the use of ACE inhibitors and diabetes were found predictive of hospital admission for COVID-19. It is demonstrated that the SARS-CoV-2 moves across species through spike glycoprotein S1, which binds to angiotensin converting enzyme 2 (ACE2) receptor present on host cells. However, many studies have been conducted to analyze this association, but the results are still not consistent [18, 50–52]. Conversely, the role of diabetes in the impairment of immune response and in the influence on COVID-19 prognosis has been widely confirmed [53, 54]. However no one of the aforementioned factors was confirmed at the multivariate analysis in our study.

Age, whose role in worsening COVID-19 clinical course has been clearly demonstrated [42], did not show any significant correlation with the symptomatic course (probable infection) or hospitalization rate in our series, probably owing to the restricted age interval of BS patients (usually 18–65 yo, according to International Guidelines).
Finally, recent studies suggested a protective role against COVID-19 of anti-influenza and anti-pneumococcal vaccines, and a role of influenza vaccination in mitigating the severity of the infection [21–23]. Nevertheless, in our series, neither in univariate nor in multivariate analysis did we observe any correlation. Interestingly, we noted an important difference in PC among our centers, which was not clearly predictable when we designed the study.

Along with the retrospective observational design of the study and the limited age range of the sample, the inter-center variability of COVID incidence represents a bias of the study. In fact, the analysis of those data that were not equally distributed among the centers (type of BS procedure, proportion of Op and C recruited) could have been affected. In particular, resizing the analysis on a smaller and more homogeneous population, the relatively higher frequency of RYGB among PC was not confirmed and some of the clinical differences between Op and C group lost significance. However, in this latter case, the trend remained and the loss of significance could be ascribed to a lower statistical power given the smaller population.

Conclusions

Despite the aforementioned limits of the study and the reduced diagnostic accuracy in an exceptional epidemic setting, patients submitted to BS seem to develop less severe SARS-CoV-2 infection than subjects with obesity. This is probably due to the improvement in obesity related comorbidities after BS, as well as to weight loss and its effects on respiratory mechanics. Further studies on larger populations could confirm the role of BS on some crucial COVID-19 outcome parameters, such as ICU admission and deaths, which were poorly represented in our series.

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Compliance with Ethical Standards

Conflict of Interest Federico Marchesi, Marina Valente, Matteo Riccò, Matteo Rottoli, Edoardo Baldini, Fouzia Mecheri, Stefano Bonilauri, Sergio Boschi, Paolo Bernante, Andrea Sciannamea, Jessica Rolla, Alice Francescato, Ruggero Bollino, Concetto Cartelli, Andrea Lanaia, Francesca Anzolin, Paolo Del Rio, Diletta Fabbì, Gabriele Luciano Petracca, Francesco Tartamella, and Giorgio Dalmonte have no conflicts of interest or financial ties to disclose.

Human and Animal Rights All procedures performed in studies involving human participants were in accordance with ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. J Am Med Assoc. 2004;292:1724–37.
2. Sjöström L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. JAMA. 2012;307:56–65.
3. Sjöström L. Review of the key results from the Swedish obese subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. J Intern Med. 2013;273:219–34.
4. Sarkhosh K, Switzer NJ, El-Hadi M, et al. The impact of bariatric surgery on obstructive sleep apnea: a systematic review. Obes Surg. 2013;23:414–23.
5. Alsumali A, Al-Hawag A, Bairdain S, et al. The impact of bariatric surgery on pulmonary function: a meta-analysis. Surg Obes Relat Dis. 2018;14:225–36.
6. Askarpour M, Khani D, Sheikhani A, et al. Effect of bariatric surgery on serum inflammatory factors of obese patients: a systematic review and meta-analysis. Obes Surg. 2019;29:2631–47.

7. van Kerkhove MD, Vandemaele KA, Shinde V, et al. Risk factors for severe outcomes following 2009 influenza A (H1N1) infection: a global pooled analysis. PLoS Med. 2011;

8. Louie JK, Acosta M, Winter K, et al. Factors associated with death or hospitalization due to pandemic 2009 influenza a(H1N1) infection in California. JAMA. 2009;302:1896–902.

9. CDC TNCPERETC. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus diseases. Vital Survelliances. 2020

10. Giangreco G. Case fatality rate analysis of Italian COVID-19 outbreak. J Med Virol. 2020;92:919–23.

11. The epidemiological characteristics of an outbreak of 2019 novel coronavirus disease (COVID-19) in China. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;

12. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA. 2020;

13. European Union. Regulation 2016/679 of the European parliament and the Council of the European Union. Off J Eur Communities. 2016;

14. Di Lorenzo N, Antoniou SA, Batterham RL, et al. Clinical practice guidelines of the European Association for Endoscopic Surgery (EAES) on bariatric surgery: update 2020 endorsed by IFSO-EC, EASO and ESPCOP. Surg Endosc. 2020;

15. Welbourn R, Pournaras DJ, Dixon J, et al. Bariatric Surgery

16. Di Lorenzo N, Antoniou SA, Batterham RL, et al. Clinical practice guidelines of the European Association for Endoscopic Surgery (EAES) on bariatric surgery: update 2020 endorsed by IFSO-EC, EASO and ESPCOP. Surg Endosc. 2020;

17. Maciejewski ML, Arterburn DE, Van Scoyoc L, et al. Bariatric surgery and long-term durability of weight loss. JAMA Surg. 2016;151:1046–55.

18. Patoulias D, Katsimardou A, Stavropoulos K, et al. Renin-angiotensin system inhibitors and COVID-19: a systematic review and meta-analysis. JCI Insight. 2016;

19. Li X, Wang Y, Agostinis P, et al. Is hydroxychloroquine beneficial for COVID-19 patients? Cell Death Dis. 2020;

20. Riccò M, Gualerzi G, Ranzieri S, et al. Stop playing with data: there is no sound evidence that bacille calmette-guérin may avoid SARS-CoV-2 infection for now. Acta Biomed. 2020;

21. Zanettini C, Omar M, Dinalankara W, Imada EL, Colantuoni E, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. Clin Infect Dis. 2020;71:889–90.

22. Centers for Disease Control and Prevention. People who are at higher risk for severe illness | CDC. Centers Dis Control Prev. 2020

23. Weisberg SP, McCann D, Desai M, et al. Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest. 2003;112:1796–808.

24. Neidich SD, Green WD, Rebjes J, et al. Increased risk of influenza among vaccinated adults who are obese. Int J Obes. 2017;41:1324–30.

25. Watson RA, Pride NB, Thomas EL, et al. Reduction of total lung volumes. Chest. 2006;130:827–34.

26. World Health Organization. Public Health Surveillance for COVID-19: Interim guidance. World Heal Organ. 2020.

27. Indagine sieroprevalenza virus Sars-Cov-2-primi-risultati [Internet]. Available from: https://statistica.regione.emiliaromagna.it/it/politiche/2020/indagine-sieroprevalenza-virus-sars-cov-2-primi-risultati

28. Registro Nazionale SICOb [Internet]. Available from: https://www.sicob.org/registro_obesi/

29. Emami A, Javanmardi F, Pirbonyeh N, et al. Prevalence of underlying diseases in hospitalized patients with COVID-19: a systematic review and meta-analysis. Arch Acad Emerg Med. 2020;

30. World Health Organization. Coronavirus disease (COVID-19) Situation Report – 162. A A Pract. 2020.

31. Rivieccio BA, Luconi E, Boracchi P, et al. Heterogeneity of covid-19 outbreak in Italy. Acta Biomed. 2020;

32. Prezioso C, Marcocci ME, Palamara AT, et al. The “Three Italy” of the COVID-19 epidemic and the possible involvement of SARS-CoV-2 in triggering complications other than pneumonia. J Neurol. 2020;26:31–23.

33. Lavezzo E, Franchin E, Ciavarella C, et al. Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo. Nature. 2020;584:425–9.

34. CDC. Coronavirus disease (COVID-19) Interim guidance. World Heal Organ. 2020.

35. Frydych LM, Bian G, O’Lone DE, et al. Obesity and type 2 diabetes mellitus drive immune dysfunction, infection development, and sepsis mortality. J Leukoc Biol. 2018;104:525–34.

36. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323:1061–6.

37. Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. Clin Infect Dis. 2020;71:889–90.

38. Regione Emilia-Romagna_Report_Coronavirus_13/10/2020.

39. Ubags NDJ, Stapleton RD, Vernooy JH, et al. Hyperleptinemia is associated with impaired pulmonary host defense. JCI Insight. 2016;

40. Watson RA, Pride NB, Thomas EL, et al. Reduction of total lung volumes. Chest. 2006;130:827–34.

41. Weisberg SP, McCann D, Desai M, et al. Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest. 2003;112:1796–808.

42. Neidich SD, Green WD, Rebjes J, et al. Increased risk of influenza among vaccinated adults who are obese. Int J Obes. 2017;41:1324–30.

43. Sheridan PA, Paich HA, Handy J, et al. Obesity is associated with impaired immune response to influenza vaccination in humans. Int J Obes. 2012;36:1072–7.

44. Centers for Disease Control and Prevention. People who are at higher risk for severe illness | CDC. Centers Dis Control Prev. 2020

45. Watson RA, Pride NB, Thomas EL, et al. Reduction of total lung capacity in obese men: comparison of total intrathoracic and gas volumes. J Appl Physiol. 2010;108:1605–12.

46. Jones RL, Nzekw MMU. The effects of body mass index on lung volumes. Chest. 2006;130:827–33.

47. Bel Lassen P, Poitou C, Genser L, et al. COVID-19 and its severity in bariatric surgery operated patients. Obesity. 2020;

48. Gianfrancesco M, Hyrich KL, Hyrich KL, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 global rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2020;79:859–66.

49. Ansarin K, Taghizadieh A, Safiri S, et al. COVID-19 outcomes in patients with systemic autoimmune diseases treated with immunomodulatory drugs. Ann Rheum Dis. 2020;annrheumdis-2020-218737.
50. Mancia G, Rea F, Ludergnani M, et al. Renin–angiotensin–aldosterone system blockers and the risk of Covid-19. N Engl J Med. 2020;382:2431–40.

51. Palazzuoli A, Mancone M, De Ferrari GM, et al. Antecedent Administration of Angiotensin Converting Enzyme Inhibitors or angiotensin II receptor antagonists and survival after hospitalization for SARS-CoV-2 (COVID-19). J Am Heart Assoc. 2020;9:e017364.

52. Flacco ME, Acuti Martellucci C, Bravi F, Parruti G, Cappadona R, Mascitelli A, et al. Treatment with ACE inhibitors or ARBs and risk of severe/lethal COVID-19: a meta-analysis. Heart [Internet]. 2020;106:1519 LP – 1524. Available from: http://heart.bmj.com/content/106/19/1519.abstract

53. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020;36

54. Burgos-Morón, Abad-Jiménez, Marañón, et al. Relationship Between Oxidative Stress, ER Stress, and Inflammation in Type 2 Diabetes: The Battle Continues. J Clin Med. 2019;8

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