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

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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 the World Health Organization criteria.

Results

In total, 353 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*), and 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

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

Key-words

Oobesity
COVID-19
SARS-CoV-2
B~~b~~ariatric surgery

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1. 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 infective 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 was 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 the Northern Italy National Healthcare System.

2. Methods

2.1. Study Ddesign and Ssetting

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 to 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.

2.2. 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].

2.3. Data Ccollection 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 Centre 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, outcome parameters.

Demographic variables included anthropometric characteristics. COPD, obstructive sleep apnea syndrome (OSAS), hypertension, diabetes, 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.

2.4. 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~~analysed~~ with the 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 case of normal distribution, or with the Mann-Whitney test, 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,"~~;~~ and "hospitalization" vs. "non--hospitalization" was initially assessed by means of the chi-square~~d~~ test, estimating the corresponding p value. All variables associated with a p value of < 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 (~~CI~~95%CI).

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 $Z\alpha$ -= -1.96, a minimum sample size of 42 participants from every center (i.e., minimum sample size of 210 participants) was calculated.

3. Results

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

In total, 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 (Ttable 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 (Ttable 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 wereas similar in the two groups too (Ttable 2).

Use of ACE inhibitors was lower in the Op group, probably owing to hypertension improvement.

Among Op patients, we recorded a lower incidence of most COVID-19-related symptoms (Ttable 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*) (Ttable 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 the 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*) (Ttable 3).

Hospitalization was more frequent in C patients (2.4% vs. 0.3%, *p*: *0.02)* as well as O_2 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%) (Ttable 3).

Univariate analysis indicated OSAS, hypertension, diabetes, pneumonia, autoimmune diseases, previous non-bariatric surgery, malignancy, and use of ACE-inhibitors as related to COVID-19 probable infection (Ttable 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*) (Ttable 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 (Ttable 4). Diabetes, hypertension, and use of ACE-inhibitors resulted as predictive factors of hospital admission (Ttable 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) (Ttable 7), while hypertension, diabetes, and use of ACE-inhibitors did not confirm to be associated with hospital admission (Ttable 7).

4. 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 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 pathogen~~et~~ic 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]. With the definition of the PC category we aimed at improving symptom~~s~~ 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] (Regione Emilia-Romagna_Report_Coronavirus_13/10/2020). 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~~behavioural~~ 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 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 [38, 39]. 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 [40]. Substantiating this, the Centers for Disease Control and Prevention considers patients with BMI ≥ 40 kg/m^2 at risk for flu complications [41–43].

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 [44, 45], 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 use of ACE inhibitors were found as predictive factors 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 co-morbidities in hospitalized patients for COVID-19 [29]. Moreover, a recent study [46] has found an association of type 2 diabetes with COVID-19 likely event in a cohort of patients undergone BS at 12 months of follow-up.

Reducing the analysis to confirmed positive cases only, autoimmune diseases alone showed a significant positive correlation, in both ~~in~~ univariate and multivariate analyse~~i~~s. However to date, available records in the literature are still not conclusive on this aspect [47, 48].

Along with BMI, use of ACE -inhibitors and diabetes were found to be predictive factors 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, 49–51]. Conversely, the role of diabetes in the impairment of immune response and in the influence on COVID-19 prognosis has been widely confirmed [52, 53]. 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 [41], 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 years old, 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 homogenous population, the relatively higher frequency of RYGB among PC was not confirmed and some of the clinical differences between the Op and C groups 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.

5. 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.

Compliance with Ethical Standards

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 was obtained from all individual participants included in the study.

Conflict of Interest

The authors declare that they have no conflict of interest.

A. Supplementary Information

ESM 1 (DOCX 27 kb).

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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/m^2; 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

Table 2. Comorbidities, therapy, and vaccinations

	Total *N* = 522		Op *N* = 353		C *N* = 169		*p* value
	N	%	*N*	%	*N*	%	
Comorbidities							
–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

Table 3. COVID-19-related symptoms, tests, and outcomes

	Total *N* = 522		Op *N* = 353		C *N* = 169		*p* value
	N	%	*N*	%	*N*	%	
Symptoms							
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							
_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	30	5.7	20	5.7	10	5.9	0.908
_Probable cases	91	17.4	51	14.4	40	23.7	0.009
Outcomes							
_Hospital admission	5	1	1	0.3	4	2.4	0.022
_O_2 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 4. Univariate analysis: characteristics by status (COVID-19 probable vs. not probable)

	Total	Probable	Not	*p*

	N = 522		*N* = 91		probable *N* = 431		value
	N	%	*N*	%	*N*	%	
≥ 60 years	253	48.5	51	56.0	202	46.9	0.111
Sex (male)	117	22.4	21	23.1	96	22.3	0.867
BMI ≥ 30 kg/m^2	341	65.3	63	69.2	278	64.5	0.389
BMI ≥ 35 kg/m^2	234	44.8	48	52.7	186	42.2	0.095
Type of surgery							
AGB	8	1.5	1	1.1	7	1.6	
RYGB	111	21.3	24	26.4	87	20.2	
SG	230	44.1	26	28.6	204	47.3	0.012
OAGB	4	0.8	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

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/m^2	341	65.3	16	53.3	325	66.1	0.155
BMI ≥ 35 kg/m^2	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	166	31.8	11	36.7	155	31.5	0.556
Diabetes (any)	65	12.5	5	16.7	60	12.2	0.471
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

Table 6. Univariate analysis: characteristics by status (hospitalization vs. no hospitalization)

	Total *N* = 522		Hospitalization *N* = 5		No hospitalization *N* = 517		*p* value
	N	%	*N*	%	*N*	%	
≥ 60 years	253	48.5	3	60.0	250	48.4	0.604
Sex (male)	117	22.4	2	40.0	115	22.2	0.343
BMI ≥ 30 kg/m^2	341	64.3	4	80.0	337	65.2	0.488
BMI ≥ 35 kg/m^2	234	44.8	4	80.0	230	44.0	0.112
Comorbidities							
COPD	35	6.7	0	-	35	6.8	0.547
OSAS	105	20.1	1	20.0	104	20.1	0.995
B-PAP/C-PAP	35	6.7	0	-	35	6.8	0.547
Hypertension	166	31.8	4	80.0	162	31.3	0.020
Diabetes (any)	65	12.5	3	60.0	62	21.0	0.001
Diabetes/oral hypoglycemic	62	11.9	3	60.0	59	11.4	0.001
Diabetes/insulin	11	2.1	0	-	11	2.1	0.742
Hypertriglyceridemia	64	12.	1	20.0	63	12.2	0.596

		3					
_Hypercholesterolemia	127	24.3	1	20.0	126	24.4	0.821
_Smoking	147	28.2	0	-	147	28.4	0.160
_Surgery (non-bariatric)	376	72.0	4	80.0	372	73.0	0.690
_Previous pneumonia	57	10.9	1	20.0	56	10.8	0.513
_Autoimmune diseases	39	7.5	1	20.0	38	7.4	0.284
_Malignancies	30	5.7	1	20.0	29	5.6	0.169
_Immune deficiencies	15	2.9	0	-	15	2.0	0.699
Therapy							
_ACE-inhibitors	75	14.4	3	60.0	72	13.9	0.003
_Colchicine	2	0.4	0	-	2	0.5	0.889
_Hydroxychloroquine	2	0.4	0	-	2	0.5	0.889
_Steroids	19	3.6	0	-	19	3.7	0.662
Vaccine							
_Seasonal flu, 2019–2020	119	22.8	1	20.0	118	22.8	0.881
_Seasonal flu, any	170	32.6	1	20.0	169	32.7	0.547
_BCG	78	14.9	1	20.0	77	14.9	0.750
_Pneumonia, any	44	8.4	0	-	44	8.5	0.495

–*BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *OSAS*, obstructive sleep apnea syndrome; *BCG*, Bacillus Calmette–Guérin

Table 7. Multivariate analysis: characteristics by status (COVID-19 “probable” vs. “not probable”; positive vs. negative; hospitalized vs. not hospitalized)

	Probable vs. not	Positive vs.	Hospitalized vs.

	probable		negative		not hospitalized	
	aOR	95%CI	aOR	95%CI	aOR	95%CI
OSAS	1.526	0.863; 2.698	-	-	-	-
Hypertension	1.849	0.993; 3.443	-	-	2.774	0.148; 52.096
ACE-inhibitors	1.751	0.869; 3.528	-	-	3.707	0.381; 36.089
Diabetes (any)	1.364	0.688; 2.704	-	-	6.511	0.861; 49.231
Surgery (non-bariatric)	1.422	0.767; 2.635	-	-	-	-
Pneumonia	3.715	1.961; 7.040	-	-	-	-
Autoimmune diseases	1.832	0.846; 3.967	3.404	1.293; 8.960	-	-
Malignancies	2.969	1.255; 7.022	-	-	-	-
Seasonal influenza 2019–2020	1.385	0.787; 2.439	-	-	-	-

OSAS, obstructive sleep apnea syndrome. Multivariate analysis through binary logistic regression; the model included all factors that in respective univariate analysis were associated with "probable" status with $p < 0.05$