COVID-19 and its Severity in Bariatric Surgery-Operated Patients

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Study importance

What is already known about this subject?

- Obesity is a major risk factor of severe forms of COVID-19 and-related mortality.
- Bariatric surgery leads to successful long-term weight loss and improvement of comorbidities that may decrease the negative outcomes of COVID-19.

What are the new findings in your manuscript?

- The prevalence of COVID-19 likely events in bariatric surgery operated patients is similar to what is observed in the general population.
- Remission of type 2 diabetes (T2D) after bariatric surgery is associated with a lower risk of COVID-19.
- A higher surgery-induced weight loss and lower weight and BMI post-surgery are associated with COVID-19 likely events.

How might your results change the direction of research or the focus of clinical practice?

- Patients post bariatric surgery, in case of non-remission of T2D should be considered at higher risk of COVID-19.
- Further research is needed to clarify the links between weight loss, malnutrition and COVID-19.

Abstract (199 words)

Objectives: Obesity is a major risk factor of severe forms of COVID-19 but little is known about the post bariatric surgery (BS) setting. We assessed the prevalence of likely COVID-19 and its risk factors in patients followed-up after BS.

Methods: We surveyed 738 patients who underwent BS and were followed-up at our university medical centre. A retrospective comparison of characteristics at baseline, one- year post BS and at the time of lockdown was performed between patients with a COVID-19 likely event (CL) based on a combination of reported symptoms vs. those for whom it was unlikely (CU).

Results: CL occurred in 62 (8.4%) patients among whom 4 (6.4%) had severe form requiring hospitalization and 1 (1.6%) died. The CL group had a higher proportion of persistent type 2 diabetes (T2D) at last follow-up (36.2% vs. 20.3%, p=0.01). BMI at the time of lockdown was lower in the CL group (30.2 ± 5.1 vs. 32.8 ± 6.5 kg/m^2; p<0.01) with higher percent weight loss since BS in the CL group. Severe forms of COVID-19 requiring hospitalization were associated with persistent T2D at last follow-up visit.

Conclusions: In post-bariatric patients, COVID-19 likely events were associated with persistent T2D and lower BMI.

Introduction

Obesity is a recognized major risk factor of severe forms of COVID-19 and related mortality, independently of obesity-associated comorbidities (1–4). Although several hypotheses have been suggested to explain why, much remains to be understood. Beyond the increased prevalence of type 2 diabetes (T2D), cardiovascular disease, alterations in respiratory function and increased risk of pulmonary embolism, the obesity-related low-grade inflammation could be an additional mechanism (5).

Bariatric surgery (BS) is increasingly performed in persons with severe obesity, especially in France which ranks third worldwide regarding the number of patients operated (6). However, very little is known on COVID-19 in post-BS patients. On the one hand, beneficial effects induced by BS could decrease patient's risk of severe COVID-19. Indeed, BS leads to successful long-term weight loss, metabolic improvement (including T2D remission) (7), improvement in sleep apnea syndrome (8) and decreased low-grade systemic inflammation (9). On the other hand, BS can lead to malnutrition and to vitamin deficiencies such as vitamin D which deficit was suggested to enhance the severity of COVID-19 (10). While recent guidelines were proposed to help prioritizing which patients could undergo bariatric and metabolic surgery during the COVID-19 pandemics (11), whether patients already operated from BS display a particular susceptibility to COVID-19 risk and severity needs urgent evaluation.

We conducted a retrospective observational study in a cohort of patients operated from BS to estimate the prevalence of COVID-19 and evaluate factors associated with COVID-19 incidence and severity in this setting.

Methods

Study population

The study is based on our ongoing BS cohort “BARICAN” of 937 patients followed-up at the Nutrition department of Pitié-Salpêtrière university hospital (Paris, France). Patients were operated in the Surgery Departments of Hôtel-Dieu, Ambroise Paré and Pitié-Salpêtrière hospitals in Paris between 2004 and 2020. Ethical approval was obtained from the French Research Ethics Committee of CPP Ile de France-1 N°13533, and by the “Commission nationale de l’informatique et des libertés” No. 1222666. Informed written consent was obtained from all subjects.

Bariatric surgery, baseline and follow-up, clinical and biological data collection

Detailed patients’ clinical, biological and anthropometric characteristics were obtained before surgery (baseline) and 12 months post-BS. T2D status were defined as proposed by the American Diabetes Association (12) at baseline, 12 months and at the last follow-up before the survey (i.e. last known T2D status). Body composition was assessed by whole-body fan-beam dual energy X-ray absorptiometry (DXA) scan (Hologic Discovery) (13). Blood samples were collected after 12-hour overnight fast. Insulin resistance was assessed by the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) (14).

Data collection during lockdown

Lockdown in France extended from March 10th up to May 11th 2020. All patients were phone-called between April 27th 2020 and May 27th 2020 and asked to contribute to a survey by answering a set of standardized questions about COVID-19, medical events and changes in lifestyle during lockdown. If the patient was unable to answer to the survey (e.g. hospitalization, death), information was gathered from relatives. A patient was considered lost to follow-up if no answer was obtained after 3 calls. A COVID-19 event was considered likely (CL) in patients who had experienced since February 2020 an episode of anosmia/dysgueusia or the association of fever (self-measured temperature ≥ 37.8°C) and one symptom among cough, dyspnea, nose discharge/swelling or odynophagia. The combination of such symptoms has been considered as most relevant for the COVID-19 likely status in recent reports (15, 16). Patients hospitalized for COVID-19 or with a positive PCR test for SARS-Cov 2 were also considered as CL. Self-measured weight before the lockdown period was recorded. Patients’ smoking and vitamin supplementation status were reported. Recent exposure defined by a close contact with a person with confirmed Sars-Cov2 infection was noted.

Statistical analysis

Continuous variables were expressed as mean ± SD. Categorical variables were expressed as absolute values and percentages. Continuous variables with a non-parametric distribution were log-transformed before analysis. Student's *t* tests for continuous variables and Pearson's chi-square ($\chi 2$) test or Fisher's exact test for categorical variables were used to compare characteristics of patients according to their COVID-19 likely status (likely or unlikely infection) i.e. CL and CU. For significant results, a multivariate logistic regression was performed adjusted on the time elapsed since surgery and last known T2D status. Significance was set at $P<0.05$. Analyses were conducted using R studio software version 1.2.1335 (http://www.r-project.org).

Results

Baseline and 12-months characteristics

From the 937 operated patients followed-up, we could collect recent information for 738 (78.8%) of them. Patients were middle-aged, mostly female and 44.0% had T2D before surgery (Table 1). The main procedures performed were Roux-en-Y gastric bypass (RYGB) (54.4%) and sleeve gastrectomy (45.0%). Only 4 (0.4%) had gastric banding. The mean time elapsed between surgery and the time of the call was 3.7 ± 2.7 years and the proportion of patients within their first year of follow-up (i.e. weight loss phase) did not differ between CL and CU groups (Table 2). Mean weight loss 1 year after surgery was close to 30% of pre-operative weight and the proportion of T2D was halved one year after surgery (Table 1).

Prevalence and factors associated with COVID-19 likely events

After BS, 62 (8.4%) patients were categorized as CL. There was no difference regarding the type of surgery or baseline characteristics between CL and CU groups. However, time elapsed since surgery was significantly higher in CL (p=0.01). One year after BS, the CL group had a higher proportion of patients with persistent T2D and higher HbA1c level (Table 1). Persistent T2D at the last follow-up visit before survey was also positively associated with CL (Table 2). BMI at the time of lockdown was lower in the CL vs. CU group with a higher percent weight loss and a lower prevalence of obesity (BMI>30 kg/m²). Importantly, in a multivariate analysis showed these differences were independent of the last known T2D status and the time since surgery (Table 2). CL patients reported more often a recent COVID-19 exposure ($p<0.01$). There was no significant difference in the vitamin supplementation status between the 2 groups.

Characteristics of the patients with severe forms of COVID-19

Among the 62 CL cases, 4 (6.4%) required hospitalization and 1 (1.6%) death was reported. Mean age was 61.8 years. Importantly, the proportion of patients with persistent T2D, was higher in patients requiring hospitalization than in those who did not: respectively, n = 4 (100%) vs. n=17 (31.4%), p=0.014.

Discussion

We surveyed a cohort of over 700 patients with history of obesity followed-up after BS to assess the prevalence of a likely COVID-19 infection (CL) in this population and describe associated characteristics. The prevalence of a CL was 8.4% among which 6.4% were severe forms requiring hospitalization. The main difference between CL vs. CU patients was a higher BS-induced weight loss and lower weight and BMI at the time of lockdown for CL. Patients likely to have had COVID-19 also had a more often persistent T2D after surgery.

This is the first study to report and describe COVID-19 cases after BS, limiting the possibility to compare with results from other countries. However, at the time of our survey, a global estimation was performed in the greater Paris region (Ile de France), area of residence of the majority of our patients, and reported an estimated prevalence of COVID-19 cases of 9.9% (17). This appears in the same magnitude as what we describe herein with a similar proportion of patients requiring hospitalization.

Type 2 diabetes is recognized as a major risk factor of severe forms of COVID-19 (18, 19) and our study suggests that this remains true after BS. Patients with persistent T2D after BS were at higher risk of COVID-19 likely events. Importantly, persistent T2D was associated with severe outcome of COVID-19.

One of the main differences observed in our likely infected patients was a lower BMI at the time of the survey which is consistent with a more important post-BS percent weight loss and this was independent of the duration of follow-up after BS. Malnutrition is known to be associated with the risk of viral pneumonia since the 1918 influenza pandemic (20) and it is possible that BS-induced malnutrition may contribute to a higher risk of infection with Sars-Cov2. Here we did not observe a difference in vitamin supplementation status between the 2 groups who also had similar vitamin levels in their one year follow-up. However, we cannot rule out differences in vitamin levels at the time of the infection.

Some limitations need to be mentioned. The definition of the COVID-19 likely events used here derives from a combination of self-reported symptoms, with a good diagnostic performance but lacks specificity (15). Another limitation is that the time elapsed between surgery and our survey was heterogeneous and significantly different between the two groups but importantly, adjustment for time since surgery did not alter our findings. Finally, potential confounders such as socio-economic status, size of family, working conditions could not be considered in this study.

Conclusion

Patients followed-up after BS displayed rates of COVID-19 likely events that appear in line with those of the general population. Persistent type 2 diabetes and lower BMI after BS is associated with the risk and the severity of COVID-19. Further work is needed to assess in more detail lifestyle changes of post-BS patients in the times of COVID-19 and the potential links between malnutrition and the risk of COVID-19.

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Table 1 Characteristics of the cohort before and 12 months after bariatric surgery according to COVID-19 likely status

	Baseline (before surgery)				**12 months after surgery**			
	All, n=738	COVID-19 unlikely, n=676	COVID-19 likely, n=62	P value	All, n=553	COVID-19 unlikely, n=501	COVID-19 likely, n=52	P value
Age (years)	50.0 (12.3)	50.1 (12.3)	49.6 (12.9)	0.77	51.0 (12.3)	51.0 (12.2)	50.7 (12.5)	0.86
Sex (male), n (%)	160 (21.7%)	148 (21.9%)	12 (19.4%)	0.76	114 (20.6%)	105 (21.0%)	9 (17.3%)	0.66
Caucasian, n (%)	611 (82.8%)	560 (82.8%)	51 (82.3%)	1.00	443 (80.1%)	401 (80.0%)	42 (80.8%)	1.00
Weight (kg)	123.6 (21.4)	123.8 (21.5)	121.7 (20.6)	0.47	88.8 (19.6)	89.1 (19.7)	85.8 (17.5)	0.21
Height (cm)	166.7 (8.6)	166.6 (8.6)	167.4 (9.3)	0.51	166.5 (8.6)	166.5 (8.6)	167.0 (9.3)	0.72
BMI (kg/m^2)	44.7 (6.6)	44.8 (6.5)	44.2 (7.2)	0.57	32.2 (6.3)	32.2 (6.2)	31.4 (7.4)	0.44
Body fat (%)	48.1 (5.1)	48.0 (5.0)	48.5 (6.1)	0.57	38.7 (6.7)	38.7 (6.6)	38.3 (7.5)	0.73
Type of surgery				1.00				1.00
Gastric banding	4 (0.5%)	4 (0.6%)	0 (0.0%)		3 (0.5%)	3 (0.6%)	0 (0.0%)	
RYGB	399 (54.4%)	365 (54.4%)	34 (54.8%)		317 (57.4%)	287 (57.4%)	30 (57.7%)	
Sleeve gastrectomy	330 (45.0%)	302 (45.0%)	28 (45.2%)		232 (42.0%)	210 (42.0%)	22 (42.3%)	
Weight loss (%)	-	-	-		28.4 (8.4)	28.3 (8.3)	29.0 (9.8)	0.64
Excess body weight loss (%)					68.6 (23.8)	68.1 (23.4)	72.6 (26.7)	0.25
Obstructive sleep apnea syndrome, n (%)	512 (73.2%)	472 (73.8%)	40 (67.8%)	0.40	201 (40.0%)	184 (40.5%)	17 (34.7%)	0.52
Hypertension, n (%)	367 (53.0%)	338 (53.1%)	29 (50.9%)	0.85	220 (39.9%)	198 (39.6%)	22 (43.1%)	0.73
Type 2 Diabetes, n (%)	308 (44.0%)	279 (43.6%)	29 (48.3%)	0.57	116 (21.0%)	97 (19.4%)	19 (36.5%)	**0.01**
Glycaemia (mmol/l)	6.2 (2.1)	6.2 (2.1)	6.7 (2.6)	0.14	5.1 (1.2)	5.0 (1.2)	5.2 (1.2)	0.58

	Baseline (before surgery)				12 months after surgery			
	All, n=738	COVID-19 unlikely, n=676	COVID-19 likely, n=62	P value	All, n=553	COVID-19 unlikely, n=501	COVID-19 likely, n=52	P value
HbA1C (%)	5.7 (0.8)	5.7 (0.7)	6.0 (1.1)	0.10	5.7 (0.8)	5.7 (0.7)	6.0 (1.1)	**0.04**
HOMA-IR	5.3 (3.7)	5.3 (3.7)	5.7 (4.0)	0.43	1.9 (1.2)	1.9 (1.2)	2.0 (1.3)	0.57
IL6 (pg/ml)	6.2 (20.7)	6.2 (21.5)	6.1 (7.3)	0.22	5.0 (18.3)	4.8 (18.1)	7.9 (19.9)	0.09
Vitamin D (ng/ml)	22.0 (10.0)	22.0 (10.2)	22.6 (8.3)	0.65	31.1 (9.3)	31.0 (9.2)	32.0 (10.1)	0.49
Vitamin B12 (pmol/l)	321 (143)	322 (137)	306 (197)	0.17	283 (149)	284 (141)	273 (212)	0.23

Results are expressed as mean (SD) for continuous data and n (%) for categorical data. P values result from Student's t test for continuous data and Chi2 or Fisher's exact test for categorical data between the 2 groups. BMI: Body Mass Index; RYGB: Roux-en-Y Gastric Bypass; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance. IL6: Interleukin 6. HbA1c : Glycated Hemoglobin A1c.

Table 2 Characteristics of the cohort at the time of lockdown according to COVID-19 likely status

	All, n=738	COVID-19 unlikely, n=676	COVID-19 likely, n=62	P value[a]	Adjusted Odd Ratio [95% CI][b]	Adjusted p value [b]
Time since surgery (years)	3.7 (2.7)	3.7 (2.7)	4.2 (2.3)	0.01	1.02 [0.92, 1.12]	0.68
Surgery <1 year ago, n (%)	81 (11.0%)	78 (11.5%)	3 (4.8%)	0.16	0.70 [0.11, 2.68]	0.65
Last known T2D status	141 (21.8%)	120 (20.3%)	21 (36.2%)	0.01	2.17 [1.20, 3.86]	<0.01
Weight (kg)	90.7 (20.4)	91.2 (20.8)	85.0 (14.6)	<0.01	0.98 [0.97, 0.99]	0.05
BMI (kg/m^2)	32.6 (6.5)	32.8 (6.5)	30.2 (5.1)	<0.01	0.92 [0.87, 0.97]	<0.01
Obesity (BMI over 30), n (%)	424 (61.7%)	396 (63.1%)	28 (47.5%)	0.03	0.52 [0.30, 0.92]	0.02
Weight loss (%)	26.3 (10.9)	26.0 (10.9)	29.3 (10.7)	0.03	1.03 [1.00, 1.06]	0.04
Excess body weight loss (%)	63.2 (27.5)	62.4 (27.7)	71.6 (24.9)	0.01	1.01 [1.00, 1.03]	0.02
Vitamin supplements, n (%)	581 (81.0%)	535 (81.4%)	46 (76.7%)	0.47	0.70 [0.36, 1.44]	0.30
Corticosteroid treatment at last visit, n (%)	16 (2.5%)	15 (2.6%)	1 (1.8%)	1.00	0.66 [0.04, 3.43]	0.70
Confirmed SarsCov-2 exposure, n (%)	135 (18.9%)	108 (16.5%)	27 (45.8%)	<0.01	5.59 [3.04, 10.3]	<0.01
Smoker, n (%)	74 (10.5%)	66 (10.2%)	8 (13.6%)	0.55	1.64 [0.68, 3.54]	0.23

Results are expressed as mean (SD) for continuous data and n (%) for categorical data. BMI: Body Mass Index

a P values result from Student's t test for continuous data and Chi2 or Fisher's exact test for categorical data between the 2 groups.

b Logistic regression adjusted for time since surgery and last known T2D status

Table 3 Characteristics of COVID-19 hospitalized patients

	COVID-19 patients requiring hospitalization N=4
Age (years)	61.8 (4.08)
Sex (male), n (%)	1 (25.0%)
Type of surgery:	
RYGB	2 (50.0%)
Sleeve	2 (50.0%)
Characteristics at 12 months after surgery	
Obstructive sleep apnea syndrome, n (%)	2 (50.0%)
Hypertension, n (%)	4 (100%)
Type 2 Diabetes, n (%)	4 (100%)
BMI (kg/m^2)	32.7 (4.60)
Body fat (%)	36.4 (12.3)
Characteristics at the time of lockdown	
Time since surgery	5.05 (1.96)
Type 2 Diabetes at last follow-up, n (%)	4 (100%)
Weight (kg)	90.5 (7.78)
BMI (kg/m^2)	30.5 (2.63)
Weight loss (%)	23.2 (0.27)
Excess body weight loss (%)	63.6 (9.73)
Death	1 (25.0%)

Results are expressed as mean (SD) for continuous data and n (%) for categorical data. BMI: Body Mass Index