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BRIEF CUTTING EDGE REPORT

Clinical Trials and Investigations

History of bariatric surgery and COVID-19 outcomes in patients with type 2 diabetes: Results from the CORONADO study

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Abstract

Objective: This study assessed the impact of a history of metabolic and bariatric surgery (MBS) on the clinical outcomes in patients with type 2 diabetes (T2D) and severe obesity hospitalized for COVID-19.

Methods: In this post hoc analysis from the nationwide observational CORONADO (Coronavirus SARS-CoV2 and Diabetes Outcomes) study, patients with T2D and a history of MBS were matched with patients without MBS for age, sex, and BMI either at the time of MBS or on admission for COVID-19. The composite primary outcome (CPO) combined invasive mechanical ventilation and/or death within 7 and 28 days following admission.

Results: Out of 2,398 CORONADO participants, 20 had a history of MBS. When matching for BMI at the time of MBS and after adjustment for diabetes duration, the CPO occurred less frequently within 7 days (3 vs. 17 events, OR: 0.15 [0.01 to 0.94], $p = 0.03$) and 28 days (3 vs. 19 events, OR: 0.11 [0.01 to 0.71], $p = 0.02$) in patients with MBS ($n = 16$) vs. controls ($n = 44$). There was no difference in CPO rate between patients with MBS and controls when matching for BMI on admission.

Conclusions: These data are reassuring regarding COVID-19 prognosis in patients with diabetes and a history of MBS compared with those without MBS.

INTRODUCTION

Soon after the beginning of the COVID-19 pandemic, people with obesity were quickly identified as being at risk for severe forms of COVID-19 (1,2). For instance, we previously reported a sevenfold increase in the risk of invasive mechanical ventilation (IMV) in individuals with BMI ≥35 kg/m^2 admitted with COVID-19 infection compared with those presenting with BMI <25 kg/m^2 (3). Management of obesity is therefore a priority to reduce the severity of COVID-19.

Metabolic and bariatric surgery (MBS) has progressively emerged as the most efficient therapeutic option for patients with severe obesity (4). Because MBS significantly reduces body weight and improves metabolic comorbidities (5), one can hypothesize that MBS may decrease the risk of severe COVID-19. Conversely, one cannot exclude that MBS can also lead to undernutrition, which could increase the severity of COVID-19 (6).

In order to further decipher the relationship between MBS and COVID-19–related outcomes, we conducted a post hoc analysis focused on CORONADO (Coronavirus SARS-CoV2 and Diabetes Outcomes) participants with a history of MBS (7).

METHODS

Study design and patients

The multicenter nationwide CORONADO study (ClinicalTrials.gov NCT04324736) is a retrospective study designed to describe the phenotypic characteristics and prognosis of patients with diabetes admitted for COVID-19 to 68 French hospitals between March 10, 2020, and April 10, 2020. The study was conducted in accordance with the Declaration of Helsinki and French legislation and approvals were obtained from the local ethics committee (IRB/IEC - GNEDS [groupe nantais d'éthique dans le domaine de la santé]; Ref.CORONADOV2), the CEREES (comité d'expertise pour les recherches, les études et les évaluations dans le domaine de la santé; *n*° INDS:1544730), and the CNIL (commission nationale de l'informatique et des libertés; DR-2020-155/920129). The design of the study has been previously reported elsewhere (7). In this ancillary study, individuals with type 1 diabetes or other causes of diabetes (including newly diagnosed diabetes) were excluded (Supporting Information Figure S1).

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Study Importance

What is already known?

- ► Obesity and type 2 diabetes are well-recognized risk factors for COVID-19 severity.
- ► Metabolic and bariatric surgery is an efficient strategy to reduce body weight and metabolic complications in severe obesity.

What does this study add?

- ► A history of metabolic and bariatric surgery may be associated with improved COVID-19 prognosis in patients with type 2 diabetes.
- ► This beneficial effect is significant only after matching on preoperative BMI and adjustment for diabetes duration.

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

- ► In the context of COVID-19 pandemic, these data suggest that the benefit–risk ratio of surgically induced body weight loss appears favorable to decrease the severity of COVID-19.
- ► Prospective studies are warranted to confirm these results in larger cohorts.

All patients with a personal history of MBS were included in the "exposed" group. These patients were matched 3:1 with other CORONADO participants without a history of MBS, according to sex, age (±3 years), and BMI (±3 kg/m²) measured either before surgery (exposed/controls, Study A) or at the time of hospital admission (exposed/controls, Study B). In the "control" group, BMI on admission was used to match both groups.

The percentage of excess weight loss (%EWL) was defined as: (weight loss/baseline excess weight) × 100. The success of MBS was defined as EWL ≥50%.

COVID-19–related outcomes

The composite primary outcome (CPO) combined IMV and/or death by day 7 (D7). A secondary time point was considered by day 28 (D28) for all patients alive and not discharged by D7 in order to consider outcomes between admission and D28.

Statistical methods

Quantitative variables are expressed using mean (SD) or median (25th to 75th percentile) and categorical variables using number

TABLE 1 Comparison of clinical characteristics before admission in patients with history of MBS (cases) and age-, sex-, and preoperative BMI-matched controls (exposed/controls, Study A)

	Available data	Exposed *n* = 16	Control *n* = 44
Clinical features			
BMI (kg/m²) (on admission)	60	33.1 ± 5.6	40.8 ± 5.6
BMI (kg/m²) (presurgery for exposed, on admission for controls)	60	41.8 ± 5.7	40.8 ± 5.6
Sex (female)	60	9 (56.3%)	26 (59.1%)
Age (y)	60	60.7 ± 10.0	60.8 ± 10.0
Diabetes characteristics			
Diabetes duration (y)	50	20 (8-28)	8 (5-16)
Hemoglobin A_{1c} (mmol/mol)	35	54.1 (43.7-64.5)	60.7 (54.1-77.6)
Hemoglobin A_{1c} (%)	35	7.1 (6.2-8.1)	7.7 (7.1-9.3)
Microvascular complications	44	7 (63.6%)	15 (45.5%)
Macrovascular complications	58	4 (25.0%)	13 (31.0%)
Treatments			
Metformin	60	4 (25.0%)	26 (59.1%)
Sulfonylurea/glinides	60	1 (6.3%)	9 (20.5%)
DPP-4 inhibitors	60	2 (12.5%)	10 (22.7%)
GLP1-RA	60	4 (25.0%)	11 (25.0%)
Insulin	60	7 (43.7%)	18 (40.9%)
Diuretics	60	6 (37.5%)	21 (47.7%)
Beta-blockers	60	3 (18.8%)	15 (34.1%)
Calcium channel blocker	60	6 (37.5%)	17 (38.6%)
ARB and/or ACE and/ or MRA	60	3 (18.8%)	11 (25.0%)
Statin	60	10 (62.5%)	19 (43.2%)
Antiplatelet agent	60	5 (31.3%)	10 (22.7%)
Anticoagulation therapy	60	1 (6.3%)	4 (9.1%)
Comorbidities			
Hypertension	60	12 (75.0%)	30 (68.2%)
Dyslipidemia	60	9 (56.3%)	20 (45.5%)
Heart failure	57	1 (6.7%)	5 (11.9%)
NAFLD	57	3 (20.0%)	6 (14.3%)
Active cancer	60	2 (12.5%)	3 (6.8%)
COPD	58	1 (6.7%)	9 (20.9%)
Treated OSA	59	4 (25.0%)	11 (25.6%)

Note: Population size was *n* = 60. Data shown are number (%) with mean ± SD or median (25th–75th percentiles) if not normally distributed. MRA includes spironolactone and eplerenone; diuretics stand here for loop diuretics, thiazide diuretics, and potassium-sparing diuretics.

Abbreviations: ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin-2 receptor blocker; COPD, chronic obstructive pulmonary disease; DPP4, dipeptidyl peptidase 4; GLP-1RA, glucagon-like peptide 1-receptor agonist; MBS, metabolic and bariatric surgery; MRA, mineralocorticoid receptor antagonist; NAFLD, nonalcoholic fatty liver disease; OSA, obstructive sleep apnea.

(%). The statistical association between two categorical variables was tested using Fisher exact test. The statistical association between binary and quantitative variables was tested using unpaired *t* test (Mann–Whitney *U* test in case of skewed distribution), and for variables with more than two categories, we used ANOVA (Kruskal–Wallis in case of skewed distribution). Confidence intervals (CI) for proportions were calculated using the Clopper–Pearson estimate.

Logistic regression models were used to calculate odds ratio (OR) associated with the different outcomes by D7. For quantitative variables, OR was expressed for an increase of 1 SD. Multiple logistic regression analyses were performed focusing on the OR associated with BMI, considering covariates identified either as clinically relevant (background knowledge) and/or significantly associated with obesity status in univariable analysis.

All statistical tests were two-sided with a type I error set at 5%, without correction for multiple testing. All analyses were performed on available data, without imputation, using statistical software R version 4.0.0.

RESULTS

Baseline characteristics of patients with history of bariatric surgery

Among 2,398 participants with T2D in the CORONADO study, 20 (0.83%) had a history of MBS, performed a median of 8.5 years (0 to 19 years) before hospital admission. The main clinical characteristics of patients with or without a history of MBS on admission are shown in Supporting Information Table S1. Patients with a history of MBS were mostly female (60%) with a mean age of 59.0 ± 10.8 years. Sixteen patients (80%) underwent a single procedure: five gastric banding (GB), five sleeve gastrectomies (SG), and six Roux-en-Y gastric bypasses (RYGB), whereas two patients underwent, respectively, two or three procedures. The success of MBS defined by EWL ≥50% was observed in eight patients (four RYGB, two GB, and two SG), whereas seven patients had a failure (three GB, two SG, two RYGB). The EWL could not be calculated in five patients because of missing data.

COVID-19–related outcomes in patients with history of bariatric surgery

By D7 following admission, 5 out of 20 patients with MBS (25%) experienced the primary composite outcome—mainly IMV (four patients, 20%)—rather than death (one patient, 5%). By D28, one additional patient died. When compared with all patients with T2D ($n = 2,378$), the rate of CPO was not statistically different between patients with or without MBS by D7 (25.0% vs. 28.7%; OR: 0.83 [0.30 to 2.29], $p = 0.72$) or D28 (25.0% vs. 35.4%; OR: 0.61 [0.22 to 1.68], $p = 0.34$).

Comparison of baseline characteristics and hospital outcomes of patients with history of MBS with patients with T2D matched for preoperative BMI

Because preoperative BMI was lacking in 4 patients, this analysis included 16 out of 20 patients (80%) with a history of MBS. Their clinical characteristics are detailed in Table 1. Patients with obesity who underwent previous MBS had lower BMI on admission than controls, confirming the persistent effectiveness of MBS on body weight loss.

When considering the occurrence of the CPO by D7 or D28, patients with a history of MBS were intubated and/or died less frequently than matched patients with T2D without a history of MBS (Table 2). After further adjustment for diabetes duration, the CPO occurred significantly less frequently in patients with a history of MBS by D7 ($p = 0.03$) and D28 ($p = 0.02$).

TABLE 2 COVID-related clinical outcomes in patients with history of metabolic and bariatric surgery (exposed) and age-, sex-, and on-admission or preoperative BMI-matched controls (exposed/controls, Study A)

Preoperative BMI-matched controls	Exposed ($n = 16$)	Control ($n = 44$)	OR (95% CI)	p value	Adjusted OR (95% CI)	Adjusted p value
Within 7 days						
Primary outcome	3 (18.8%)	17 (38.6%)	0.37 (0.08-1.34)	0.13	0.15 (0.01-0.94)	0.03
Death	1 (6.23%)	4 (9.1%)	0.67 (0.03-4.97)	0.72	NC	NC
IMV	2 (12.5%)	14 (31.8%)	0.31 (0.04-1.30)	0.11	0.20 (0.01-1.39)	0.09
Within 28 days						
Primary outcome	3 (18.75%)	19 (43.18%)	0.30 (0.06-1.11)	0.07	0.11 (0.01-0.71)	0.02
Death	1 (6.25%)	7 (15.91%)	0.35 (0.02-2.23)	0.30	NC	NC
IMV	2 (12.5%)	15 (34.09%)	0.28 (0.04-1.17)	0.08	0.21 (0.01-1.39)	0.09

Note: Categorical data are presented using *n* (%). *P* values are calculated using likelihood ratio test, unadjusted and adjusted on diabetes duration logistic regression.

All patients with personal history of MBS were included in the "exposed" group. These patients were matched 3:1 with other CORONADO participants without history of MBS, according to sex, age (±3 years), and BMI (±3 kg/m²) measured either before surgery (exposed/controls, Study A) or at the time of hospital admission (exposed/controls, Study B).

Abbreviations: IMV, invasive mechanical ventilation; NC, algorithm did not converge and OR was not estimated.

TABLE 3 Comparison of clinical characteristics before admission in patients with history of MBS (cases) and age-, sex-, and on-admission BMI-matched controls.

	Available data	Exposed $n = 20$	Control $n = 58$
Clinical features			
BMI (kg/m²) (on admission)	78	33.1 ± 5.4	33.0 ± 5.0
BMI (kg/m²) (presurgery for exposed, on admission for controls)	75	42.3 ± 5.9	33.0 ± 5.0
Sex (female)	78	12 (60.0%)	34 (58.6%)
Age (y)	78	59.0 ± 10.8	59.8 ± 9.7
Diabetes characteristics			
Diabetes duration (y)	65	20 (7 to 30)	7 (2-16)
Hemoglobin A_{1c} (mmol/mol)	55	59.6 (46.5-69.4)	61.8 (52.7-72.1)
Hemoglobin A_{1c} (%)	55	7.6 (6.4-8.5)	7.8 (7.0-8.8)
Microvascular complications	63	8 (57.1%)	19 (38.8%)
Macrovascular complications	76	4 (20.0%)	15 (26.8%)
Treatments			
Metformin	78	7 (35.0%)	42 (72.4%)
Sulfonylurea/glinides	78	1 (5.0%)	16 (27.6%)
DPP-4 inhibitors	78	3 (15.0%)	9 (15.5%)
GLP1-RA	78	4 (20.0%)	9 (15.5%)
Insulin	78	8 (40.0%)	19 (32.8%)
Diuretics	78	6 (30.0%)	18 (31.0%)
Beta-blockers	78	5 (25.0%)	19 (32.8%)
Calcium channel blocker	78	7 (35.0%)	24 (41.0%)
ARB and/or ACE and/or MRA	78	5 (25.0%)	16 (27.6%)
Statin	78	11 (55.0%)	30 (51.7%)
Antiplatelet agent	78	7 (35.0%)	25 (43.1%)
Anticoagulation therapy	78	1 (5.0%)	2 (3.5%)
Comorbidities			
Hypertension	77	14 (70.0%)	46 (80.7%)
Dyslipidemia	78	11 (55.0%)	37 (63.8%)
Heart failure	74	1 (5.3%)	7 (12.7%)
NAFLD	75	3 (15.8%)	6 (10.7%)
Active cancer	77	2 (10.0%)	4 (7.0%)
COPD	76	1 (5.3%)	3 (5.3%)
Treated OSA	69	4 (21.1%)	7 (14.0%)

Note: Population size was $n = 78$. Data shown are number (%) with mean ± SD or median (25th–75th percentiles) if not normally distributed. MRA includes spironolactone and eplerenone. Diuretic stands here for loop diuretics, thiazide diuretics, and potassium-sparing diuretics.

Abbreviations: ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin-2 receptor blocker; COPD, chronic obstructive pulmonary disease; DPP4, dipeptidyl peptidase 4; GLP-1RA, glucagon-like peptide 1-receptor agonist; MBS, metabolic and bariatric surgery; MRA, mineralocorticoid receptor antagonist; NAFLD, nonalcoholic fatty liver disease; OSA, obstructive sleep apnea.

Comparison of baseline characteristics and hospital outcomes of patients with history of MBS with patients with type 2 diabetes matched for BMI on admission

The second ancillary analysis included all patients ($n = 20$) with a history of MBS and 58 patients with T2D matched for age, sex, and on-admission BMI (33.1 ± 5.4 vs. 33.0 ± 5.1 kg/m^2) (Table 3). The rates of death and IMV were not statistically different between the two groups within D7 and D28 after admission. The results were similar after further adjustment for diabetes duration (Table 4).

DISCUSSION

In this observational study, we found that a history of MBS was associated with a better prognosis in sex-, age-, and BMI-matched patients with T2D hospitalized for COVID-19 during the same time period.

TABLE 4 COVID-related clinical outcomes in patients with history of metabolic and bariatric surgery (exposed) and age-, sex-, and on-admission BMI-matched controls (exposed/controls, Study B)

Admission BMI-matched controls	Exposed (*n* = 20)	Controls (*n* = 58)	OR (95% CI)	*p* value	Adjusted OR (95% CI)	Adjusted *p* value
Within 7 days						
Primary outcome	5 (25.0%)	22 (37.9%)	0.55 (0.16-1.63)	0.29	0.39 (0.08-1.54)	0.12
Death	1 (5.0%)	1 (1.7%)	0.33 (0.01-8.7)	0.45	NC	NC
IMV	4 (20%)	21 (36.2%)	0.44 (0.11-1.39)	0.17	0.43 (0.08-1.68)	0.16
Within 28 days						
Primary outcome	5 (25.0%)	23 (39.7%)	0.51 (0.15-1.51)	0.23	0.34 (0.07-1.29)	0.09
Death	2 (10.0%)	6 (10.3%)	0.96 (0.13-4.63)	0.96	0.22 (0.01-1.98)	0.56
IMV	4 (20.0%)	21 (36.2%)	0.44 (0.11-1.39)	0.17	0.44 (0.09-1.72)	0.16

Note: Categorical data are presented using *n* (%). *P* values are calculated using likelihood ratio test, unadjusted and adjusted on diabetes duration logistic regression.

All patients with personal history of MBS were included in the "exposed" group. These patients were matched 3:1 with other CORONADO participants without history of MBS, according to sex, age (±3 years), and BMI (±3 kg/m^2) measured either before surgery (exposed/controls, Study A) or at the time of hospital admission (exposed/controls, Study B).

Abbreviations: IMV, invasive mechanical ventilation; NC, algorithm did not converge and OR was not estimated.

Even if the underlying mechanisms remain to be fully elucidated, the association of class II/III obesity with the more severe forms of COVID-19 is now well established (8,9). A large body of evidence has also shown that T2D is an independent risk factor for SARS-CoV-2 infection and COVID-19 severity (7,10,11). By surveying a single-center bariatric cohort during the first lockdown, Bel Lasem et al. found that COVID-19–likely events were associated with lower BMI at the time of the lockdown and a higher surgery-induced weight loss in patients with a history of MBS, suggesting that MBS could be detrimental regarding COVID-19 prognosis (12). In contrast, retrospective studies based on the post hoc analysis of electronic records suggested that MBS may be protective against severe forms of SARS-CoV-2 infection. In a nationwide French medico-administrative study, a history of MBS was independently associated with a significant reduction in the risk of mortality in individuals with obesity who developed COVID-19 infection (OR 0.50; 95% CI: 0.31-0.80; $p < 0.01$) (13). In the United States, Aminian et al. found a reduced need for hospitalization in 33 patients with a history of MBS compared with 330 matched controls with class II/III obesity but no history of MBS (14). In addition, a retrospective observational study suggested that patients submitted to MBS ($n = 353$) develop less severe COVID-19 infection than patients with obesity waiting for MBS ($n = 169$) (15).

Although observational, the CORONADO study has several strengths. First, although no previous study has specifically analyzed the impact of MBS on COVID-19 outcome in T2D, it should be noted that the proportion of patients with a history of MBS in our study population (0.8%) was in agreement with the expected proportion of operated patients in people with T2D in France (16,17). Second, we showed that participants with a history of MBS presented with slightly lower hemoglobin A_{1c} and glycemia on admission. This latter finding suggests that MBS is able to counterbalance the burden of diabetic complications on COVID-19 outcomes (8,18).

Some limitations should be mentioned. The most obvious is the observational design of our study, the low number of patients with MBS, the low number of CPO events (especially regarding deaths), and the absence of randomization between exposed and unexposed patients, which makes the control of confounding factors uncertain. Also, we did not account for multiple testing. Finally, substantial data were missing, such as preoperative BMI, which could not be documented in four patients (20%).

CONCLUSION

In conclusion, our study suggested that a history of MBS in patients with obesity and T2D and hospitalized for COVID-19 might be associated with a better prognosis than in those without MBS. Prospective studies are needed to confirm these results in larger populations in order to further promote efficient weight loss interventions as therapeutic strategy to improve COVID-19 prognosis in patients with severe obesity.O

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CONFLICT OF INTEREST

EB-C reports grants, nonfinancial support, or personal fees from Fujirebio, NovaBiomedica, and Siemens Healthineers. LB reports grants, nonfinancial support, or personal fees from AstraZeneca, Becton Dickinson, BMS, Boehringer Ingelheim, Eli Lilly, Janssen, MSD, Novartis, Novo Nordisk, Pierre Fabre Santé, Roche, and Sanofi. SB reports grants, nonfinancial support, or personal fees from Abbott, Boehringer Ingelheim, Eli Lilly, Medtronic, Medtrum, Novartis, and Novo Nordisk. CC reports grants, nonfinancial support, or personal fees from Eli Lilly, Novo Nordisk, and Sanofi. MP reports grants, nonfinancial support, or personal fees from Air Liquid, Allergan, Amgen, Elivie, Fortil, Lifescan, NHC, Novo Nordisk, and Sanofi. MW reports personal fees from Novo Nordisk. SH reports grants, nonfinancial support, or personal fees from Air Liquid, Allergan, AstraZeneca, Bayer, Boehringer Ingelheim, Dinno Santé, Eli Lilly, Elivie, Fortil, Lifescan, LVL, Merck Sharpe Dome, NHC, Novartis, Pierre Fabre Santé, Sanofi, Servier, and Valbiotis. PG reports grants or personal fees from Abbott, Air Liquid, Allergan, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Lifescan, Merck Sharp and Dohme, Mundipharma, Novo Nordisk, Sanofi, and Servier. BC reports grants, nonfinancial support, or personal fees from Abbott, Amgen, Akcea AstraZeneca, Pierre Fabre, Genfit, Gilead, Eli Lilly, Merck Sharpe Dome, Novo Nordisk, Regeneron, and Sanofi. The other authors declared no conflict of interest.

AUTHOR CONTRIBUTIONS

CB, BC, and FP had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: BC, FP, CB. Acquisition, analysis, or interpretation of data: CB, BC, PG, BGu, SH, FP, MP, SS, TP, MW. Critical revision of the manuscript for important intellectual content: all coauthors. Statistical analysis: TP, MW. Patient recruitment: LB, SB, OB, CC, CC-B, BGa, NG, CG-L, LM, GP, RR, DS-B, CT, BT, BV.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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