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Effect of bariatric surgery on lung function and asthma control after 8 years of follow-up

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ABSTRACT

Background: Bariatric surgery has a proven beneficial effect on asthma symptoms and lung function in patients with class III obesity and asthma. The effects of bariatric surgery on asthma control and small airway function persist for at least 12 months after bariatric surgery. However, long-term follow-up data are lacking.

Objectives: To evaluate the very-long term effects of bariatric surgery on asthma symptoms and lung function.

Methods: In a prospective, longitudinal follow-up study, we planned an 8-year follow-up visit for patients previously included in the OBAS 1.0 trial, which evaluated the effects of bariatric surgery on asthma control and lung function in patients with asthma and class III obesity in The Netherlands.

Results: Fifteen of 78 patients from the OBAS trial completed the 8-year follow-up visit. Nine patients underwent bariatric surgery, and six patients did not. After 8 years of follow-up, asthma control (Asthma Control Questionnaire [ACQ] score at 12 months of 0.4 versus an ACQ score of 0.7 at 8 years of follow-up; $p=0.075$) and small airway function (R_5-R_{20} (frequency-dependent resistance at 5Hz–20Hz); score at 12 months of 0.25 versus an ACQ score of 0.07 at 8 years of follow-up; $p=0.345$) remained clinically stable compared with 12 months of follow-up. Patients who underwent bariatric surgery had a statistically significant weight regain between 12 months of follow-up and 8 years of follow-up (median [interquartile range] body mass index 30.2 kg/m² [23.9–43.4 kg/m²] versus 32.3 kg/m² [24.0–36.4 kg/m²]; $p=0.025$). However, the impact of weight regain on asthma control, and asthma quality of life was clinically insignificant (ACQ, β (regression coefficient) = 0.04; 95% Confidence Interval [0.02; 0.06]; $p<0.001$; and AQLQ; $\beta = -0.04$ CI [−0.07; −0.009]; $p=0.013$).

Conclusion: These results emphasize the importance of bariatric surgery in treating obesity-related asthma.

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Obesity is associated with an increased risk of developing asthma.¹ This obesity-related asthma phenotype is difficult to control and less responsive to standard asthma therapy.^{2–4} The pathophysiology of this phenotype is not fully understood, although mechanical and inflammatory factors have been suggested.^{5–9} We previously (OBAS trial, NTR3204) demonstrated that weight loss by bariatric surgery improves asthma control by increasing lung function and reducing airway hyperreactivity in the short term

(up to 12 months).^{10,11} So far, long-term data after bariatric surgery are not available. Here, we complement our previously published short-term data with 8-year follow-up data, which focused on asthma symptoms, lung function, and body mass index (BMI).¹⁰

METHODS

Study Design

This prospective longitudinal follow-up study was conducted at a center of excellence for asthma and chronic obstructive pulmonary disease in The Netherlands.¹ The study protocol and 1-year follow-up results of the OBAS 1.0 trial have been published.¹⁰ The follow-up study (OBAS 1.1) was open for inclusions between November 2017 and June 2018. All participating patients gave written informed consent.

The study protocol was approved by the medical ethics committee (Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. 2017-69; Netherlands Trial Register NL.62822.101.17)

Study Patients

Two groups of patients from the OBAS 1.1 study were invited for an 8-year follow-up visit: patients

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with asthma who underwent bariatric surgery (BS group) and those with asthma who did not undergo bariatric surgery (NBS group).¹⁰ The inclusion and exclusion criteria of the OBAS 1.0 trial¹⁰ have been reported. Patients were excluded from the study if they were pregnant, were initially included in the non-asthma control group, or were initially included in the NBS groups but had undergone bariatric surgery between the 12-month and 8-year visits. All the patients received usual care according to Global Initiative for Asthma (GINA) guidelines¹² between the OBAS 1.1 trial and this 8-year follow-up trial.

Outcomes

The study’s primary end point was the score change in the Asthma Control Questionnaire (ACQ) and Asthma Quality of Life Questionnaire (AQLQ) between 12 months and 8 years of follow-up after bariatric surgery.^{13,14} Secondary study parameters were lung function, airway resistance, physical activity, and obesity parameters.

Assessments. Description of pulmonary function tests (spirometry, lung volumes, exhaled nitric oxide, impulse oscillometry), questionnaires (ACQ and AQLQ), measurements of physical activity, and laboratory tests were described in the previous study.¹⁰

Statistics

For the comparison between the two groups at baseline, the independent samples median test for scaled data or the χ^2 test or Fisher exact test were used. For all groups, 12-month follow-up data were compared with

8-year follow-up data by using the related-samples Wilcoxon rank test. The impact of bariatric surgery and asthma on the outcomes over time (baseline, 12 months; follow-up, 8 years) was studied by using repeated measurements analysis (linear mixed modeling). For the impact of BMI on ACQ and AQLQ scores, and lung function, BMI was included as a covariable instead of bariatric surgery in the repeated-measurements analysis. Paired data for scale variables are expressed as median (minimum-maximum), and categorical variables are expressed as percentages. All analyses were performed by using SPSS V.25.0 software. Results were evaluated at 95% confidence interval (CI) at a two-sided significance threshold of $p < 0.05$.

RESULTS

Of the 78 patients who had a completed follow-up of 12 months in the initial study of OBAS 1.0, 15 patients with asthma (6 in the NBS group and 9 in the BS group) could be included in the study (Fig. 1). The baseline characteristics of the patients are shown in Table 1. The study’s main findings are summarized in Fig. 2 and Table 2.

Asthma Control and Asthma Quality of Life

In all the groups, the improvements in ACQ scores at 1 year were still present after 8 years (Fig. 2 a; Appendix A). The median AQLQ score after 8 years was significantly lower in the BS group versus 12 months (6.2 versus 6.7; $p = 0.030$). However, the median change was not clinically relevant (Δ AQLQ score – 0.34 versus MCID of 0.5). There was no difference in ACQ and AQLQ scores was observed between the BS

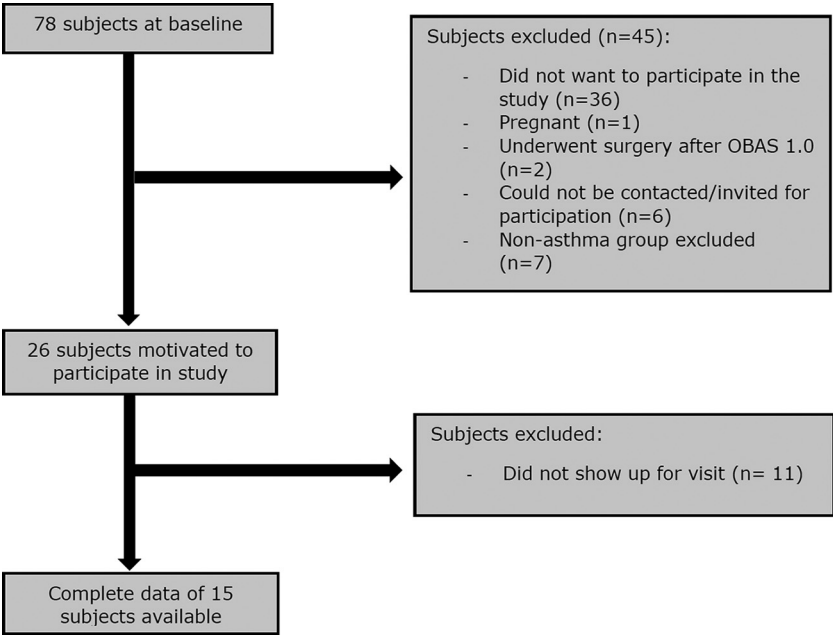


Figure 1. Flowchart of study participants.

Table 1 Baseline characteristics

Characteristic	Baseline		8-Year Follow-up	
	NBS + Group (n = 12)	BS + Group (n = 27)	NBS + Group (n = 6)	BS + Group (n = 9)
Women, %	91.7	74.1	83.3	77.8
Non-white ethnicity, %	25.0	14.8	0.0	11.1
Age, median (minimum-maximum), y	33 (20–45)	36 (19–48)	41 (28–53)	49 (33–56)
Smoking status, %				
Never smoked	75.0	55.6	83.3	50.0
Smoked in history	16.7	11.1	16.7	12.5
Current smoker	8.3	33.3	0.0	37.5
Age of onset of asthma as child, %	75	33	66.7	33.3
Inhaled corticosteroids, %	21.4	17.2	66.7	11.1

NBS = No bariatric surgery and asthma; A = Asthma; BS = bariatric surgery and asthma.

and NBS groups (ACQ score, β -0.43 [95% CI, -1.2 ; 0.35], $p=0.255$; and AQLQ score, β 0.11 [-0.69 ; 0.91], $p=0.780$) (Fig. 2 *a, b*). Both ACQ and AQLQ scores were significantly associated with BMI during follow-up. However, the impact was minimal and not clinically relevant. (for ACQ score, β 0.04 CI [0.02 ; 0.06], $p<0.001$; for AQLQ score, β -0.04 CI [-0.07 ; -0.009], $p=0.013$).

Lung Function

After 8 years, the median forced expiratory volume in the first second of expiration (FEV₁ post bronchodilator) in the BS group was significantly higher compared with the median FEV₁ at 12 months. In addition, the median FEV₁ in the BS group was significantly higher compared with the NBS group during 12 months of follow-up (β -11.28 [-20.34 ; -2.21]; $p=0.020$) (Fig. 2 *c*). A higher BMI was significantly associated with a lower FEV₁ (β -0.59 [-0.97 ; -0.21]; $p=0.003$). No difference was observed in changes of FEV₁/forced vital capacity (FVC) between asthma groups (β -0.09 CI [-1.91 ; 2.09]; $p=0.924$) over time (Fig. 2 *d*). No significant association was found between BMI and FEV₁/FVC (β -0.14 CI [-0.29 ; 0.02]; $p=0.080$). The improvement in small airway function (R₅-R₂₀) in the first 12 months after surgery persisted after 8 years of follow-up. Moreover, the R₅-R₂₀ in the patients with asthma who underwent bariatric surgery was significantly lower during 8 years of follow-up compared with patients with asthma who did not undergo bariatric surgery (β -0.08 CI [0.004 ; 0.16]; $p=0.041$) (Fig. 2 *e*). In addition, R₅-R₂₀ was significantly associated with BMI (β 0.006 CI [0.004 ; 0.008]; $p<0.001$).

Body Composition

After 8 years, the median BMI was significantly higher compared with 12 months of follow-up in the

BS group (Appendix A). However, 8 years after bariatric surgery, the BMI was still significantly lower compared with the BMI before surgery (45.1 kg/m² versus 32.3 kg/m²; $p=0.012$). In the BS group, the percentage of fat mass increased significantly between the 1-year and 8-year visits (36.0% versus 42.9% (36.0% at the 1-year visit versus 42.9% at the 8-year visit), $p=0.018$), whereas the absolute increase in fat mass did not reach statistical significance (31.3 kg versus 39.6 kg (31.3 kg at the 1-year visit and 39.6 kg at the 8-year visit); $p=0.063$). Patients with asthma who underwent bariatric surgery had a persistent lower BMI during 8 years of follow-up compared with patients with asthma who did not undergo bariatric surgery (β -12.35 CI [-15.93 ; -8.77]; $p<0.001$).

Activity

Despite the initial increase in total daily steps at 12 months after bariatric surgery, the median of total daily steps in both bariatric groups was lower at 8 years compared with 12 months of follow-up. This difference was not statistically significant, nor did we observe statistically significant differences in the total number of steps between the BS and NBS groups in the multivariable analysis (Fig. 2 *g*).

DISCUSSION

We demonstrated that the positive effects of bariatric surgery on asthma-related outcomes in patients with class III obesity and asthma persisted 8 years after surgery. Asthma control in both groups remained stable during 8 years of follow-up after bariatric surgery, and, although there was a decrease in asthma-related quality of life in the BS group, this was not clinically relevant. This is interesting, because, in our first paper on this topic, we noted that the ACQ score

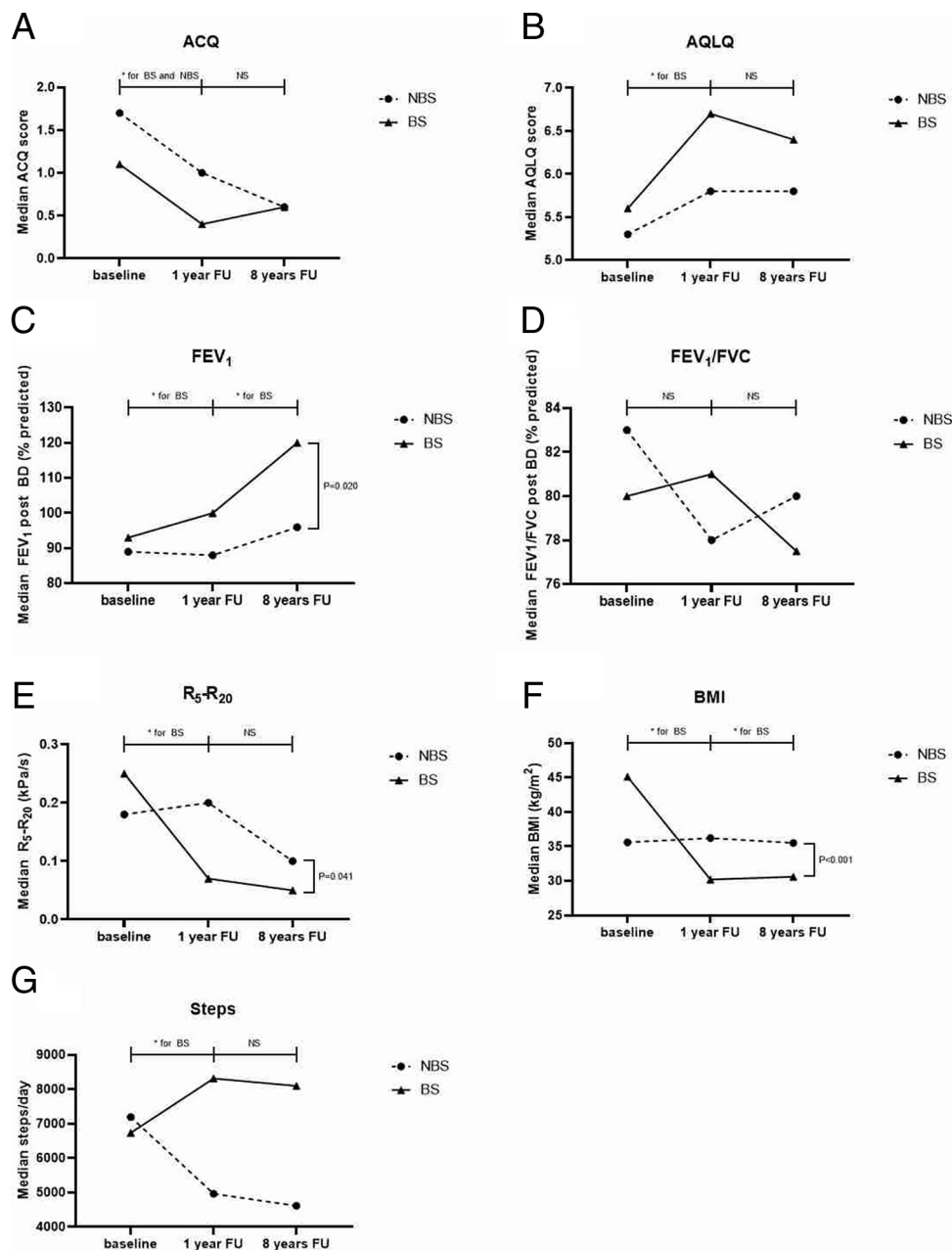


Figure 2. Effect of weight loss by bariatric surgery on (a) asthma control (ACQ), (b) asthma quality of life (AQLQ), (c) FEV₁, (d) FEV₁/FVC, (e) airway resistance (R₅-R₂₀), (f) BMI, and (g) total daily steps during 8 years of follow-up. NBS group (circles); BS group (triangles). The horizontal line at the top of every graphs represent the *p*-values for comparison between baseline and 12-month follow-up, and *p* values for comparison between 12-month and 8-year follow-up; only significant *p* values are shown (*). On the side: *p* values for the difference between the groups over time (repeated measurements [mixed model]); only significant *p* values are shown. ACQ = Asthma Control Questionnaire; AQLQ = Asthma Quality of Life Questionnaire; FEV₁ = forced expiratory volume in the first second of expiration; FVC = forced vital capacity; R₅-R₂₀ =; BMI = body mass index; NBS = no bariatric surgery and asthma; BS = bariatric surgery and asthma.

promptly improved in both groups (BS and NBS groups) after inclusion, whereas the AQLQ score improved in the BS group only.¹⁰ In a previous study, increased BMI was associated with lower (worse) AQLQ scores.¹⁵ Therefore, the significant increase in AQLQ scores in the BS group was most likely caused by weight loss, which eventually leads to a higher health-related quality of life. Subsequently, we postulated that weight regain after bariatric surgery might worsen the AQLQ score. It did, but the absolute change was not clinically significant (AQLQ $\beta = -0.04$ CI [-0.07; -0.009]; $p = 0.013$), which suggests that other health-related factors

contribute to the worsening of the health-related quality of life.

In the BS group, there was an increase in median BMI after 8 years, but this increase did not return to the baseline BMI. Another important finding is that, despite the increase in BMI, the improvement in small airway function (R₅-R₂₀) in the BS group persisted after 8 years of follow-up. The outcomes of this study contribute to the limited knowledge about the long-term effects of bariatric surgery in patients with class III obesity and asthma. A study by Hewitt *et al.*¹⁶ evaluated the long-term effects of bariatric surgery on pulmonary function and asthma control. After 5 years of follow-up, they

Table 2 Detailed descriptives of study outcomes

Group	NBS + A group				BS + A Group					
	Baseline (n = 12)	12-mo follow-up (n = 12)	8-year follow-up (n = 6)	p*	p#	Baseline (n = 27)	12-mo follow-up (n = 27)	8-year follow-up (n = 9)	p*	p#
Weight, kg	103 (82–133)	107 (82–136)	103 (98–118)	0.173	0.028	130 (101–202)	88 (68–144)§	89 (69–131)	0.108	0.012
BMI, kg/m ²	35.6 (30.9–53.9)	36.2 (31.8–55.0)	35.5 (32.7–38.7)	0.116	0.028	45.1 (38.1–63.8)	30.2 (23.9–43.4)§	32.3 (24.0–36.4)	0.025	0.012
Abdominal circumference, cm	119 (102–155)	113 (95–135)	111 (43–120)	0.500	0.465	133 (112–165)	99 (90–142)§	97 (84–131)	0.733	0.018
VVM	56.3 (43.0–70.9)	56.0 (42.7–67.9)	58.2 (51.7–71.9)	0.043	0.068	61.2 (47.8–100.5)	49.0 (41.5–79.12)§	48.6 (43.8–76.1)	0.866	0.028
VVMI	19.5 (16.7–22.8)	18.8 (17.3–23.6)	19.2 (18.1–22.2)	0.043	0.144	21.5 (17.1–31.0)	17.8 (15.6–22.9)§	18.2 (15.3–19.8)	0.204	0.028
Body fat, %	43.5 (24.5–59.5)	43.5 (26.2–59.8)	43.3 (28.0–46.4)	0.144	0.068	50.9 (37.6–70.4)	36.0 (19.9–52.0)§	42.9 (31.3–47.0)	0.018	0.018
Total fat weight, kg	45.1 (27.6–79.0)	43.3 (29.2–81.0)	42.5 (33.1–51.8)	0.043	0.068	68.1 (44.5–134.4)	31.3 (14.2–67.60)§	39.6 (22.0–45.4)	0.063	0.018
Steps	7191 (3307–9587)	4964 (2021–12176)	4613 (2061–10083)	0.317	0.655	4964 (2021–12176)	8312 (3030–12910)§	5977 (3192–9106)	0.465	1.000
Asthma										
ACQ	1.7 (0.3–2.6)	1.0 (0.3–2.0)§	0.6 (0.3–1.9)	0.248	0.043	1.1 (0.4–2.9)	0.4 (0.0–1.9)§	0.7 (0.0–2.0)	0.075	0.075
AQLQ	5.3 (0.0–6.7)	5.8 (3.4–6.7)	5.8 (5.3–6.1)	0.116	0.080	5.6 (3.7–6.8)	6.7 (3.0–7.0)§	6.2 (4.8–7.0)	0.030	0.110
Lung function										
Spirometry										
FEV ₁ , pre, % predicted	91 (45–106)	81 (71–117)	91 (79–108)	0.141	0.891	86 (66–119)	95 (67–119)§	102 (77–116)	0.089	0.018
FEV ₁ , post, % predicted	98 (49–106)	88 (70–118)	96 (83–112)	0.138	0.458	93 (75–118)	100 (79–117)§	119 (76–121)	0.046	0.018
FVC, pre, % predicted	103 (64–118)	103 (77–131)	107 (83–119)	0.138	0.893	97 (75–126)	105 (75–131)§	120 (78–133)	0.075	0.028
FVC, post, % predicted	104 (62–120)	106 (78–131)	105 (85–121)	0.138	0.686	99 (74–126)	107 (77–123)§	121 (76–136)	0.115	0.018
FEV ₁ /FVC, pre, %	79 (61–90)	78 (63–83)	78 (69–83)	0.588	0.892	76 (63–92)	77 (57–92)	73 (64–86)	0.683	0.734
FEV ₁ /FVC, post, %	83 (69–91)	78 (66–86)	80 (74–85)	0.276	0.683	80 (67–94)	81 (69–94)	78 (72–86)	0.498	0.056
RV, post, % predicted	80 (74–92)	80 (51–105)	75 (64–99)	0.498	0.180	74 (39–126)	84 (40–115)	89 (55–109)	0.207	0.917
TLC, post, % predicted	93 (77–109)	97 (74–107)	97 (80–102)	0.465	0.317	97 (83–106)	102 (79–115)§	106 (70–114)	0.673	0.345
FRC, post, % predicted	68 (54–90)	69 (40–87)	63 (52–80)	0.080	0.180	59 (40–95)	91 (53–135)§	102 (55–118)	0.933	0.058
RV/TLC, post, %	27 (20–36)	23 (18–40)	26 (15–34)	0.077	0.317	22 (10–41)	25 (13–36)	27 (14–37)	0.596	0.465
FEV ₁ reversibility, %'	7 (–12–22)	4 (–4–12)	4 (–1–11)	0.686	0.893	9 (–6–20)	8 (–5–27)	5 (–2–20)	0.933	0.090
FeNO, ppb	16 (7–96)	15 (8–58)	21 (6–69)	0.416	0.144	16 (8–45)	15 (8–36)	19 (11–33)	0.345	0.715
IOS										
R _s , kpa/sec	0.58 (0.24–1.11)	0.62 (0.29–0.86)	0.41 (0.31–0.70)	0.500	0.068	0.69 (0.42–1.39)	0.42 (0.26–0.80)§	0.35 (0.24–0.67)	0.866	0.028
R ₂₀ , kpa/sec	0.44 (0.20–0.65)	0.40 (0.21–0.64)	0.29 (25–0.60)	0.138	0.138	0.45 (0.27–1.03)	0.32 (0.20–0.61)§	0.31 (0.19–0.38)	0.735	0.018
R ₅ –R ₂₀ , kpa/sec	0.18 (0.04–0.62)	0.20 (0.07–0.27)	0.10 (0.05–0.25)	0.225	0.500	0.25 (0.06–0.66)	0.07 (0.01–0.19)§	0.05 (0.03–0.24)	0.345	0.028
Frequency response (Fres), Hz	17.3 (9.2–30.4)	17.6 (10.9–24.8)	13.6 (9.5–21.7)	0.043	0.686	22.7 (10.5–29.0)	11.9 (5.9–23.1)§	10.0 (8.47–24.45)	0.612	0.043

NBS + = No Bariatric Surgery; BS = bariatric surgery; A = ; BMI = body mass index; FFM = Fat Free Mass; FFM = Fat Free Mass Index; ACQ = Asthma Control Questionnaire; AQLQ = Asthma Quality of Life Questionnaire; FEV₁ = forced expiratory volume in the first second of expiration; pre = pre bronchodilator; post = post bronchodilator; FVC = forced vital capacity; RV = ; TLC = ; FRC = Functional residual capacity; FeNO = Fractional exhaled Nitric Oxide; IOS (IOS) = Impulse Oscillometry; R_s = Resistance at 5 Hz; R₂₀ = Resistance at 20 Hz; Fres = Frequency response.

*The p value for the comparison between the 12-mo follow-up and 8-year follow-up within each group.

#The p value for the comparison between baseline and 8-year follow-up within each group.

\$A p < 0.05 for the comparison baseline vs 12-mo follow-up within each group.

reported considerable improvements in asthma symptoms in 48% of the patients. However, the asthma diagnosis and the evaluation of symptoms were based on patient self-reported outcome measures without additional objective measurements. Another study, by Maniscalco *et al.*,¹⁷ found significant improvements in asthma control after 1 and 5 years of bariatric surgery compared to patients with asthma without bariatric surgery. In contrast to the present study, they found a sustained decrease in the BMI between 1 year and 5 years of follow-up after bariatric surgery. However, the improvements in FEV₁ and FVC values in patients with asthma who underwent bariatric surgery were only significant after 5 years of follow-up. In the present study, FEV₁, FVC, and lung volumes (Residual Volume (RV); Total Lung Capacity (TLC); Functional residual capacity (FRC); Air Trapping (RV/TLC)) were improved after 12 months in the BS group, and the improvements persisted over the years. In fact, the median FEV₁ post bronchodilator in the BS group was significantly higher at the 8-year follow-up compared with 12 months of follow-up. No significant improvement in FEV₁/FVC values was found in the BS group, which indicated that bariatric surgery did not influence large airway obstruction in the long term in this group of patients. A meta-analysis confirmed this finding.¹⁸ Although Maniscalco *et al* found a significant increase in BMI, we showed that BMI was not significantly associated with FEV₁/FVC. In contrast, the present study showed a sustained improvement in R₅-R₂₀, a marker of small airway function, in the BS group. Given the significant correlation of R₅-R₂₀ with BMI, it is likely that small airways play an essential role in obesity-related asthma.^{19,20} This study adds to earlier literature, because we included a control group of patients with asthma and obesity who did not undergo bariatric surgery. This study had some limitations: (1) some patients could not be contacted due to outdated patient details; (2) the participation rate was low; of the 26 patients who were initially invited, only 15 patients showed up; the small sample size could result in bias; and (3) we did not perform a methacholine provocation test to measure bronchial hyperreactivity.

CONCLUSION

Bariatric surgery has a long-lasting effect on BMI, lung function, and small airway function. Although there was some relapse in terms of weight gain, BMI remained significantly lower compared with baseline values. All findings together emphasize the importance of bariatric surgery in treating obesity-related asthma.

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