

# Predictive Factors for Insufficient Weight Loss After Bariatric Surgery: Does Obstructive Sleep Apnea Influence Weight Loss?

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## Abstract

**Background** Important endpoints of bariatric surgery are weight loss and improvement of comorbidities, of which obstructive sleep apnea (OSA) is the highest accompanying comorbidity (70 %). This study aimed to evaluate the influence of OSA on weight loss after bariatric surgery and to provide predictive factors for insufficient weight loss (defined as  $\leq 50$  % excess weight loss (EWL)) at 1 year follow-up.

**Methods** All consecutive patients, who underwent primary laparoscopic Roux-en-Y gastric bypass or laparoscopic sleeve gastrectomy between 2006 and 2014 were retrospectively reviewed. Patients with data on preoperative apnea-hypopnea index (AHI) and pre- and postoperative body mass index (BMI) were included. After surgery, the percentage excess weight loss (%EWL) and BMI changes were compared between preoperatively diagnosed OSA-, subdivided in mild, moderate, and severe OSA, and non-OSA patients.

Multivariable logistic regression analysis evaluated predictive factors for  $\leq 50$  % EWL.

**Results** A total of 816 patients, 522 (64 %) with and 294 (36 %) without OSA, were included. After 1 year, OSA patients achieved less %EWL than non-OSA patients (65.5 SD 20.7 versus 70.3 SD 21.0;  $p < 0.01$ ). The lowest %EWL was seen in severe OSA patients (61.7 SD 20.2). However, when adjusted for waist circumference, BMI, and age, no effect of OSA was seen on %EWL or changes in BMI. Although AHI, gender, age, BMI, type of surgery, and type II diabetes were predictive factors for  $\leq 50$  % EWL (area under the curve 0.778), the AHI as variable was of little importance.

**Conclusions** The presence of OSA does not individually impair weight loss after bariatric surgery.

**Keywords** Bariatric surgery · Obstructive sleep apnea · Excess weight loss · Continuous positive airway pressure

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## Abbreviations

AHI	Apnea-hypopnea index
BMI	Body mass index
CPAP	Continuous positive airway pressure
(%) EWL	Percentage excess weight loss
LRYGB	Laparoscopic roux-en-Y gastric bypass
LSG	Laparoscopic sleeve gastrectomy
OSA	Obstructive sleep apnea
PG	Polygraphy
PSG	Polysomnography

## Introduction

Obesity affects more than one third of the North-American population [1] and has proven to be a threat to human health as it predisposes for metabolic syndrome, cardiovascular diseases, and other comorbidities [2]. Since bariatric surgery is the only proven effective therapy for morbid obesity concerning weight loss and improvement of comorbidities on the long term, it is not surprising that the number of bariatric procedures has increased enormously in the last decade.

The two most performed bariatric procedures are the laparoscopic Roux-en-Y gastric bypass (LRYGB; 47 %) and laparoscopic sleeve gastrectomy (LSG; 28 %) [3]. These procedures result in 66 and 59 % excess weight loss (%EWL), respectively [4, 5].

Despite these good long-term results, it is estimated that 10–20 % of patients show insufficient weight loss [6–8]. Although little is known about predictive factors for insufficient weight loss, the problem is thought to be multifactorial, including medical, surgical, and psychological aspects [8]. Several articles reported a possible association between suboptimal weight loss and high preoperative body mass index (BMI), personality disorders, and diabetes mellitus [6, 9–11]. A previous published multivariable logistic regression analysis showed that young patients with a lower BMI and higher waist circumference achieved more %EWL after 1 year and the success percentage of more than 60 % EWL was higher [12]. Another study revealed that early postoperative weight loss predisposes the eventual result as patients who achieved less than 30 % EWL after 6 months were not likely to achieve more than 50 % EWL after 2 years [13].

Although some predictive factors were found for insufficient weight loss after bariatric surgery, many factors that are common in bariatric surgery patients have not been fully investigated yet. One of them includes obstructive sleep apnea (OSA), one of the highest accompanying comorbidities [14, 15]. Ravesloot et al. performed a prospective observational study in which all patients scheduled for bariatric surgery underwent mandatory polysomnography (PSG). With an absolute incidence of 70 %, it was concluded that OSA is under recognized and underdiagnosed in patients undergoing

bariatric surgery [14]. The advantages of bariatric surgery regarding OSA are described by the systematic review and meta-analysis of Buchwald et al., showing decrease in severity of OSA in 80 % of the patients after surgery [16].

However, other studies suggest that OSA itself may cause weight gain in the non-bariatric population due to an associated relationship with obesity, comorbidities, and other physiological and metabolic diseases [17]. This could be a result of reduced physical activity and subtle hormonal (leptine and ghrelin) disturbances, leading to an increased appetite [18].

So, while obesity might lead to OSA, OSA might also induce weight gain. To what extent OSA is a risk factor for insufficient weight loss after bariatric surgery is unknown. Therefore, the primary aim of this study is to investigate the %EWL and changes in BMI between OSA and non-OSA patients 6 months to 1 year after bariatric surgery. Secondary aims are examining the influence of both OSA severity and CPAP compliance on weight loss and to provide predictive factors for insufficient weight loss (defined as  $\leq 50$  % EWL) after 1 year follow-up.

## Methods

### Study Design and Study Population

A retrospective study was performed with a hospital database in which all patients scheduled for bariatric surgery in the Sint Lucas Andreas Hospital (SLAZ) were entered consecutively. All patients met the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) criteria [19] for bariatric surgery. Patients who underwent primary LRYGB or LSG where considered eligible for inclusion. They were included in this study when the following data were available: (1) Length, preoperative weight, and preoperative AHI data and (2) Postoperative weights at 6 months to 1 year follow-up. Exclusion criteria were other bariatric procedures, such as laparoscopic adjustable gastric banding (LAGB), revisional surgery from previous bariatric procedures or unavailable data regarding P(S)G and/or pre- and postoperative weights.

### Surgical Procedures

All LRYGB and LSG procedures were performed by four experienced bariatric surgeons or under their direct supervision, using a standardized technique. Five trocars were used for surgery. The LRYGB consists of two anastomosis, of which the proximal gastrojejunostomy (GJ) was created by the gastric pouch, consisting of an estimated 30-ml volume, and the proximal jejunal limb, whereas the distal jejunojunostomy (JJ) was created at an estimated 120–150-cm distance from the GJ. Both anastomoses were made using staplers and VICRYL 2.0 (Ethicon inc. a Johnson and Johnson

Company, Somerville, NY, USA) or a V-Loc™ (Covidien, Dublin, Ireland). The LSG was performed with staplers using a 34F nasogastric tube as boogie size. The remnant stomach was removed. Desufflation and skin closure followed after both procedures.

### Evaluation Obstructive Sleep Apnea

Preoperative P(S)G provided the apnea-hypopnea index (AHI), classifying the OSA severity. An AHI of 0–5 states no OSA, whereas 5–15, 15–30, and  $\geq 30$  states mild, moderate, and severe OSA, respectively. Before 2012, preoperative P(S)G was not performed routinely, whereas from 2012 onwards, all patients who were scheduled for bariatric surgery underwent mandatory P(S)G, preoperatively. Since a PSG not only provides the AHI, but also includes a hypnogram showing the sleep cycles, REM sleep, deep sleep, arousal index and awakings, PSG was preferably performed. However, due to cost reasons, many patients underwent polygraphy (PG) that provided the AHI without showing a hypnogram. In case of moderate to severe OSA (AHI  $\geq 15$ ), CPAP therapy was prescribed. AHI on CPAP was registered, as well as mean duration of CPAP use per night. Patients were considered CPAP dependent when using the therapy for more than 4 h a night, at least 70 % of the nights [20]. After surgery, patients with severe OSA were continuously monitored at the Intensive Care Unit during the first night, whereas all other patients (AHI 0–30) were admitted to the bariatric surgical ward for standard intermittent monitoring. If CPAP therapy was prescribed in patients with an AHI between 15 and 30, they were required to bring their CPAP mask to the bariatric surgical ward for mandatory usage.

### Weight Loss

The primary endpoint of this study is the %EWL after 6 months and 1 year of follow-up. This was calculated based on the pre- and postoperative BMI at 6 months and 1 year after bariatric surgery. Changes in BMI were calculated and displayed as differences in BMI points.

### Data Collection and Statistical Analysis

Required data were retrieved from patient medical records. The retrieved baseline characteristics included gender, age, preoperative BMI, waist circumference, type of surgery, type II diabetes, hypertension, dyslipidemia, alcohol, and smoking. Continuous characteristics of OSA and non-OSA patients were documented with mean/standard deviation and compared with the independent *t* test. Normality was evaluated with histograms and the Kolmogorov-Smirnov test. Categorical variables were compared with chi-square test. In addition, baseline characteristics were compared between all

OSA severity groups with one-way ANOVA. Homogeneity of variance between groups (ANOVA assumption) was tested by using Levene's test. Comparison of %EWL and BMI changes were primarily completed between non-OSA (AHI < 5) and OSA (AHI  $\geq 5$ ) groups with the independent *t* test. Analysis for %EWL and BMI changes between all OSA severity groups was achieved with one-way ANOVA with post hoc analysis and Bonferroni correction. Potential influence of confounders was investigated with covariance analysis. Within the CPAP group, comparison of %EWL and BMI changes between compliant and non-compliant patients was achieved with independent *t* test.

Finally, correlations between AHI and %EWL and loss of BMI points were analyzed with Pearson's correlation coefficients. A prediction model for insufficient %EWL, defined as  $EWL \leq 50$  %, was created by multivariable logistic regression analysis according to the TRIPOD statement [21].

All data were anonymously entered in a database. The local ethical committee of the Director board of the SLAZ provided approval for this study.

## Results

### Patient Characteristics

From November 2007 until January 2014, 1594 patients underwent bariatric surgery. Of these patients, 973 underwent primary LRYGB or primary LSG. After excluding 157 patients (16 %) due to missing data, concerning P(S)G, and/or weight data, a total of 816 patients were included for analysis. OSA was diagnosed in 522 (64 %) patients, of which 163 (31 %) had a severe form.

The mean AHI of the entire study population was 18.9 (24). Patients without OSA had a mean AHI of 2.3 (1.5), whereas patients with OSA had a mean AHI of 28.2 (25.6). Mild, moderate, and severe OSA patients had an AHI of 9 (2.8), 21.2 (4.2), and 59.4 (24.2), respectively. A total of 275 (33.7 %) patients received CPAP therapy prior to surgery. Significant differences between OSA and non-OSA patients were found for the variables gender, age, preoperative BMI, waist circumference, type II diabetes, hypertension, and dyslipidemia. Baseline characteristics and their comparisons among the different OSA groups are shown in Table 1.

### Influence of OSA on Weight Loss

Six months after bariatric surgery, the entire study population showed a mean EWL of 54.1 % (16.9) (Table 2). A trend was seen towards less %EWL in patients with OSA when compared to patients without OSA (53.2 versus 55.6 %;  $p=0.058$ ).

One year post-surgery, mean EWL of the whole cohort was 67.2 % (20.9). Significant less %EWL was seen in OSA

**Table 1** Comparison of baseline characteristics—OSA and non-OSA patients

Variables	All patients <i>n</i> =816	No OSA AHI<5 <i>n</i> =294	OSA AHI≥5 <i>n</i> =522	<i>p</i> value	Mild OSA AHI 5–15 <i>n</i> =209	Moderate OSA AHI 15–30 <i>n</i> =150	Severe OSA AHI≥30 <i>n</i> =163	<i>p</i> value*
Gender; <i>n</i> (%)				<0.01 <sup>a</sup>				<0.01 <sup>a</sup>
Female	654 (80.1)	272 (92.5)	382 (73.2)		187 (89.5)	115 (76.7)	80 (49.1)	
Male	162 (19.9)	22 (7.5)	140 (26.8)		22 (10.5)	35 (23.3)	83 (50.9)	
Age; years (SD)	44.4 (10.6)	39.7 (9.8)	47.1 (10.2)	<0.01 <sup>b</sup>	44.3 (10.6)	47.8 (9.6)	49.9 (9.2)	<0.01 <sup>c</sup>
Preoperative BMI; kg/m <sup>2</sup> (SD)	45.8 (6.7)	44.4 (5.7)	46.5 (7.2)	<0.01 <sup>b</sup>	45.3 (6.4)	46.2 (7.2)	48.4 (7.7)	<0.01 <sup>c</sup>
Waist circumference; cm (SD)	131.5 (15.2) ( <i>n</i> =718)	126.9 (13.4) ( <i>n</i> =264)	134.2 (15.5) ( <i>n</i> =454)	<0.01 <sup>b</sup>	129 (14.1) ( <i>n</i> =194)	135.1 (15) ( <i>n</i> =127)	140.9 (15.6) ( <i>n</i> =133)	<0.01 <sup>c</sup>
Type of surgery; <i>n</i> (%)				0.127 <sup>a</sup>				0.221 <sup>a</sup>
LRYGB	766 (93.9)	281 (95.6)	485 (92.9)		198 (94.7)	137 (91.3)	150 (92)	
LSG	50 (6.1)	13 (4.4)	37 (7.1)		11 (5.3)	13 (8.7)	13 (8)	
Type II diabetes; <i>n</i> (%)	250 (30.6)	61 (20.7)	189 (36.2)	<0.01 <sup>a</sup>	54 (25.8)	60 (40)	75 (46)	<0.01 <sup>a</sup>
Hypertension; <i>n</i> (%)	359 (44)	90 (30.6)	269 (51.5)	<0.01 <sup>a</sup>	86 (41.1)	82 (54.7)	101 (62)	<0.01 <sup>a</sup>
Dyslipidemia; <i>n</i> (%)	227 (27.9)	61 (20.8)	166 (31.8)	<0.01 <sup>a</sup>	51 (24.4)	48 (32)	67 (41.1)	<0.01 <sup>a</sup>
Alcohol; <i>n</i> (%)	332 (42)	128 (44.3)	204 (40.6)	0.316 <sup>a</sup>	77 (37.4)	66 (45.8)	61 (40.1)	0.319 <sup>a</sup>
Smoking; <i>n</i> (%)				0.311 <sup>a</sup>				0.698 <sup>a</sup>
Yes	156 (19.5)	62 (21.5)	94 (18.4)		36 (17.6)	26 (17.8)	32 (20.1)	
Former	173 (21.7)	55 (19)	118 (23.1)		49 (23.9)	30 (20.5)	39 (24.5)	

AHI apnea-hypopnea index, BMI body mass index, LRYGB laparoscopic Roux-en-Y gastric bypass, LSG laparoscopic sleeve gastrectomy, OSA obstructive sleep apnea

<sup>a</sup> Chi-square test

<sup>b</sup> Independent *t* test

<sup>c</sup> One-way ANOVA

\**p* value between all OSA severity groups, including no-, mild-, moderate-, and severe OSA

patients when compared to non-OSA patients (65.5 versus 70.3 %; *p*<0.01).

At both intervals, %EWL was significantly different between patients without OSA, mild OSA, moderate OSA, and severe OSA (*p*<0.01). After 6 months, post hoc analysis with correction for multiple testing showed that this was a result of

a significant difference of %EWL between patients without OSA and those with severe OSA (*p*<0.01). Comparing mild and moderate OSA patients with severe OSA patients revealed post hoc *p* values of 0.058 and 0.056, respectively. At 1 year follow-up, post hoc analysis as previously described showed significantly less %EWL in severe OSA patients

**Table 2** Weight Loss in OSA and non-OSA patients displayed in %EWL and changes in BMI

Variables	All patients	No OSA AHI 0–5	OSA AHI≥5	<i>p</i> value	Mild OSA AHI 5–15	Moderate OSA AHI 15–30	Severe OSA AHI≥30	<i>p</i> value**
%EWL 6 months (SD)	54.1 (16.9)	55.6 (16.2)	53.2 (17.2)	0.058 <sup>a</sup>	54.6 (17.3)	55.0 (17.8)	49.9 (16.3)	<0.01 <sup>b</sup>
Adjusted*	–	52.1	–	–	53.7	57.2	55.7	0.015
%EWL 1 year (SD)	67.2 (20.9)	70.3 (21.0)	65.5 (20.7)	<0.01 <sup>a</sup>	68.5 (20.9)	65.4 (20.5)	61.7 (20.2)	<0.01 <sup>b</sup>
Adjusted*	–	66.6	–	–	67.9	68.7	68.0	0.781
BMI <sup>Δ</sup> 6 months (SD)	10.7 (3.1)	10.4 (3.0)	10.8 (3.1)	0.049 <sup>a</sup>	10.6 (3.0)	11.0 (3.0)	11.0 (3.4)	0.120 <sup>b</sup>
BMI <sup>Δ</sup> 1 year (SD)	13.3 (4.1)	13.1 (4.0)	13.4 (4.1)	0.466 <sup>a</sup>	13.3 (3.9)	13.1 (3.9)	13.6 (4.6)	0.592 <sup>b</sup>

AHI apnea-hypopnea index, EWL excess weight loss, FU follow up, OSA obstructive sleep apnea, SD standard deviation

<sup>a</sup> Independent *t* test

<sup>b</sup> One-way ANOVA

\*%EWL adjusted for waist circumference, BMI and age (*n*=689)

\*\**p* value between all OSA severity groups, including no-, mild-, moderate- and severe OSA; Homogeneity of variances; Levene’s test *p*>0.05

<sup>Δ</sup> Changes in BMI points

when compared with patients without OSA ( $p<0.01$ ) and those with mild OSA ( $p=0.015$ ).

Three confounders, including waist circumference, BMI, and age, influenced these results. When adjusted for these confounders, a significant difference between OSA severity groups was found 6 months after surgery ( $p=0.015$ ), whereas this difference was not presented anymore at 1 year follow-up ( $p=0.781$ ). In all OSA severity groups, the expected increase of %EWL was significant between 6 months and 1 year after surgery ( $p<0.01$ ).

In addition to the %EWL, changes in BMI were calculated. After 6 months, mean BMI loss was 10.7 (3.1). After 1 year, mean BMI loss was 13.3 (4.1). No clinical significant difference was found between OSA and non-OSA patients, or between all OSA severity groups at both intervals (Table 2).

The AHI and %EWL showed a Pearson correlation of  $-0.149$  ( $p<0.01$ ) and  $-0.184$  ( $p<0.01$ ) after 6 months and 1 year, respectively. The %EWL decreases as AHI increases. At 6 months, a higher AHI resulted in less BMI changes (Pearson correlation 0.105;  $p=0.003$ ). No significance level was reached after 1 year (Pearson correlation 0.06;  $p=0.097$ ).

### Influence of CPAP Compliance on Weight Loss

Preoperatively, CPAP was prescribed in 275 OSA patients (52.7 %), of which 4 (1.9 %), 112 (74.7 %), and 159 (97.5 %) patients were diagnosed with mild, moderate, and severe OSA, respectively. The four patients with mild OSA received CPAP treatment due to clinical symptoms or severe positional OSA, meaning the AHI increases when a patient sleeps in supine position. This number ( $n=4$ ) was too small to analyze the effect of CPAP compliance on %EWL and these four patients were therefore excluded from analysis. Postoperative CPAP compliance was objectified in 140 moderate and severe patients. Compliance reports were not available for 131 patients. Reasons were returned CPAP devices without previous compliance reports, no response of the patients after repeated invitations for follow-up or prescribed CPAP elsewhere.

The mean AHI on CPAP was 3.8 (3.9). Median duration per night of CPAP usage was 224 (520) minutes. No difference in %EWL or BMI loss between compliant and non-compliant CPAP use was found in both moderate and severe OSA patients (Table 3). Although a positive correlation was found between average minutes CPAP use and %EWL at 6 months (Pearson correlation 0.196,  $p=0.040$ ), no correlation was detected after 1 year of follow-up ( $p=0.113$ ). In addition, no significant correlation was found between average CPAP use and BMI changes at both follow-up moments ( $p=0.318$  and  $p=0.641$ , respectively).

### Weight Loss and Postoperative AHI 6 Months and 1 Year After Bariatric Surgery

Preoperatively, a total of 522 patients had OSA, of which the median AHI was 18.9 (144). Six months after bariatric surgery, 112 moderate and severe OSA (35.8 %) patients repeated their P(S)G, showing a significant decrease of the median AHI to 10.4 (IQ range 14.4;  $p<0.01$ ). OSA (AHI  $\geq 5$ ) was still present in 86 (76.8 %) patients, showing a median AHI of 13.4 (IQ range 15.5). Consequently, 26 patients had remission of OSA (AHI 2.9; IQ range 1.8). Patients with persistent OSA had similar %EWL as those with remission of OSA (51.8 SD 15.8 versus 57.1 SD 15.1,  $p=0.131$ ). In addition, mean BMI loss was also comparable between groups (11.2 SD 3.1 versus 11.2 SD 2.9;  $p=0.995$ ).

Of the 112 moderate and severe OSA patients who repeated P(S)G, 76 patients (67.9 %) were downgraded to no or mild OSA and no longer required CPAP therapy. Consequently, 36 patients (32.1 %) still had an AHI above 15, requiring CPAP therapy.

One year after surgery, 55 patients repeated their P(S)G, showing a median AHI of 7.5 (IQ range 9.8). These P(S)Gs revealed that OSA still existed in 38 (69 %) patients, whereas remission was reported in 17 (31 %) patients. The AHI of these groups were 10.1 (91) and 2.7 (4.7), respectively. No significant difference of %EWL was seen between patients with remission of OSA and those with persistent OSA (64.7 SD 15.9 versus 57 SD 17.8;  $p=0.123$ ). In addition, no difference regarding BMI changes was detected between persistent OSA (13 SD 5.5) and cured OSA (13.7 SD 3.4) patients ( $p=0.574$ ).

Of the 55 moderate and severe OSA patients repeating P(S)G after 1 year, the AHI downgraded below 15 in 42 patients (76.4 %), who consequently no longer required CPAP therapy. An AHI above 15 was still presented in 13 patients (26.3 %) who were advised to continue CPAP therapy.

### Predictors for Insufficient Weight Loss After Bariatric Surgery ( $\leq 50$ % EWL)

A total of 149 (19.7 %) patients had less than 50 % EWL 1 year after bariatric surgery. In univariate logistic regression analysis, variables gender, age, BMI, waist circumference, AHI, type II diabetes, hypertension and dyslipidemia reached a  $p$  value of  $<0.1$  (Table 4).

Multivariable logistic regression analysis evaluated predictive factors for  $\leq 50$  % EWL, 1 year after bariatric surgery. All characteristics, including gender, age, preoperative BMI, waist circumferences, AHI, type of surgery, type II diabetes, hypertension, dyslipidemia, alcohol, and smoking were

**Table 3** Weight loss in CPAP compliant and non-compliant patients

Variables	Moderate OSA; CPAP compliant (n=20)	Moderate OSA; CPAP non-compliant (n=41)	p value	Severe OSA; CPAP compliant (n=26)	Severe OSA; CPAP non-compliant (n=53)	p value
%EWL 6 months	55.9 (18.9 <sup>a</sup> )	55.3 (18.8 <sup>a</sup> )	0.944 <sup>b</sup>	50.8 (15.4 <sup>a</sup> )	48.8 (17.5 <sup>a</sup> )	0.620 <sup>b</sup>
%EWL 1 year	67.4 (21.4 <sup>a</sup> )	66.8 (21.4 <sup>a</sup> )	0.454 <sup>b</sup>	61.4 (17.1 <sup>a</sup> )	61.7 (20.2 <sup>a</sup> )	0.950 <sup>b</sup>
BMI <sup>Δ</sup> 6 months	10.6 (3.3 <sup>a</sup> )	10.7 (2.7 <sup>a</sup> )	0.918 <sup>b</sup>	11.5 (3.0 <sup>a</sup> )	10.9 (3.8 <sup>a</sup> )	0.438 <sup>b</sup>
BMI <sup>Δ</sup> 1 year	12.5 (3.8 <sup>a</sup> )	13.3 (4.0 <sup>a</sup> )	0.915 <sup>b</sup>	13.9 (3.5 <sup>a</sup> )	13.8 (4.9 <sup>a</sup> )	0.930 <sup>b</sup>

AHI apnea-hypopnea index, CPAP continuous positive airway pressure, EWL excess weight loss, OSA obstructive sleep apnea

<sup>a</sup> Standard deviation

<sup>b</sup> Independent t test

<sup>Δ</sup> Changes in BMI points

analyzed. All continuous variables were linear related to the outcome.

Multivariable analysis with backward selection resulted in the elimination of the variables waist circumference, smoking, hypertension, dyslipidemia, and alcohol, consecutively. The optimal prediction model included gender, age, preoperative BMI, preoperative AHI, type of surgery, and type II diabetes (Nagelkerke R square 0.208, Hosmer and Lemeshow test  $p=0.443$ , AUC 0.77, Fig. 1) (Table 5).

**Table 4** Univariate logistic regression analysis—predictors for  $\leq 50$  % EWL

Variable	$\leq 50$ % EWL - 1 year after bariatric surgery		
	OR	95 % CI	p value
Gender			
Female			
Male	1.711	1.127–2.600	0.012
Age; years	1.024	1.006–1.041	0.008
Preoperative BMI; kg/m <sup>2</sup>	1.127	1.095–1.159	0.000
Waist circumference; cm	1.047	1.033–1.061	0.000
AHI	1.011	1.004–1.017	0.002
Type of surgery	3.864		
LRYGB			
LSG		2.122–7.037	0.000
Type II diabetes	1.723	1.186–2.504	0.004
Hypertension	1.395	0.974–1.999	0.069
Dyslipidemia	1.623	1.107–2.379	0.013
Alcohol	1.129	0.780–1.635	0.519
Smoking			
Yes	0.812	0.490–1.346	0.419
Former	1.091	0.695–1.711	0.705

AHI apnea-hypopnea index, BMI body mass index, CI confidence interval, EWL excess weight loss, LRYGB laparoscopic Roux-en-Y gastric bypass, LSG laparoscopic sleeve gastrectomy, OR odds ratio, OSA obstructive sleep apnea

## Discussion

### Study Population

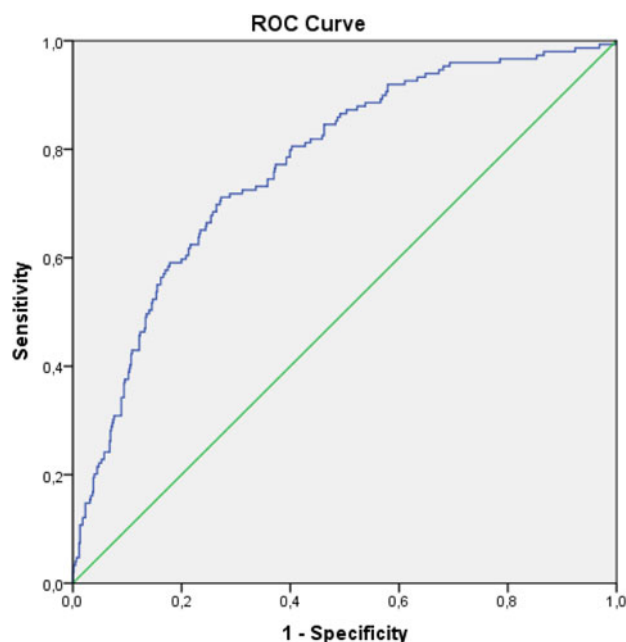
In this bariatric surgery population, OSA was diagnosed by P(S)G in 522 (64 %) patients, of which 163 (31 %) suffered of a severe form. This high rate is in agreement with literature, showing a prevalence of 70 and 40 %, respectively [14].

### The Role of OSA in Weight Loss After Bariatric Surgery

After bariatric surgery, a significant difference in %EWL between OSA severity groups was seen at both 6 months and 1 year follow-up. These differences were caused by a lower %EWL in severe OSA patients. However, these results were not significant after adjusting for waist circumference, BMI, and age. In combination with many significant differences in baseline characteristics of OSA severity groups, less %EWL is likely to be caused by higher BMI (correlation  $-0.478$ ;  $p<0.01$ ); higher waist circumference (correlation  $-0.381$ ;  $p<0.01$ ); older age (correlation  $-0.098$ ;  $p<0.01$ ); presence of type II diabetes (mean EWL 63.1 % SD 20.9 versus 69.0 % SD 20.7;  $p<0.01$ ); hypertension (mean EWL 65.3 % SD 21.7 versus 68.7 % SD 20.2;  $p=0.028$ ); and dyslipidemia (mean EWL 63.6 % SD 21.3 versus 68.6 % (20.6);  $p<0.01$ ). Therefore, it can be concluded that the less %EWL in OSA patients compared to non-OSA patients is more accountable to its accompanying characteristics than to the AHI itself. Furthermore, no difference regarding BMI changes was detected between patients with and without OSA. Results of this study imply that the importance of OSA regarding weight loss is weak and perhaps transient.

However, moderate and severe OSA patients were treated with CPAP, which reduces the AHI below five. It could be hypothesized that when CPAP is compliantly used, OSA itself no longer influences the %EWL or changes in BMI. The effect of CPAP compliance is therefore an interesting topic for future prospective studies. Although no difference was detected between CPAP compliant and non-compliant OSA patients

**Fig. 1** ROC curve for prediction model for insufficient ( $\leq 50\%$  EWL) weight loss



Area under the curve: 0.771  
Standard Error: 0.021  
 $p < 0.01$   
95% C.I. 0.729–0.812

in this study, a weak positive correlation was found between average CPAP use and %EWL 6 months after surgery. This implies that more compliant CPAP use provides more %EWL. However, CPAP compliance was not always objectified during the relevant follow-up period, but at a random period after surgery. This may influence results, as CPAP compliance may vary during follow-up. In addition, no correlation was detected between average CPAP use and %EWL or changes in BMI, 1 year post-surgery. In order to conclude whether CPAP compliance has a significant effect on weight loss, prospective studies are required evaluating the mean compliance during the relevant follow-up period.

**Table 5** Multivariable logistic regression analysis—predictors for  $\leq 50\%$  EWL

Variable	$\leq 50\%$ EWL - 1 year after bariatric surgery		
	OR	95 % CI	$p$ value*
Gender; F/M			
Male	1.645	0.934–2.868	0.080
Age; years	1.035	1.011–1.058	0.003
BMI; $\text{kg}/\text{m}^2$	1.148	1.108–1.190	0.000
AHI	0.992	0.982–1.002	0.117
Type of surgery; LRYGB/LSG			
LSG	1.961	0.918–4.187	0.082
Type II diabetes	1.921	1.199–3.076	0.007

Nagelkerke  $R^2 = 0.208$

AHI apnea-hypopnea index, BMI body mass index, CI confidence interval, EWL excess weight loss, LRYGB laparoscopic Roux-en-Y gastric bypass, LSG laparoscopic sleeve gastrectomy

\*Hosmer and Lemeshow test:  $p > 0.05$

While a significant correlation of AHI and %EWL was found, Pearson's  $\rho$  was only  $-0.185$ , implying a weak correlation. In univariate analysis, the AHI explained 2 % of  $\leq 50\%$  EWL after 1 year follow-up. One of the limitations of the present study is the discrepancy between the performance of PSG and PG due to cost reasons. There can be substantial differences in AHI between PSG and PG. As PSG includes sleep/wake periods, the total AHI is based on the AHI in sleeping periods, whereas PG measures the average AHI during the whole night without differentiating between sleep/wake periods. Since the AHI is zero during wake periods, patients who underwent PG instead of PSG may have a reported AHI that underestimated the true AHI. For this reason, a subanalysis was performed. Of 816 included patients, 476 (58.3 %) and 324 (39.7 %) underwent PG and PSG, respectively. Differentiation between PG and PSG was not possible in 16 patients in whom sleep study was performed elsewhere. Median AHI of PG and PSG was 6.3 (IQ range 15.1) and 14.5 (IQ range 29.5), respectively ( $p < 0.01$ ). Although the performance of PG and PSG might have introduced selection bias to this study, this probably has no effect on current study conclusions. The effect of OSA on %EWL is probably even less than accounted for in the current study, as patients who underwent PG have an underestimated AHI. Moreover, this would be the only selection bias as all patients, including those with and without symptomatic OSA, underwent sleep registration prior to surgery from 2012 onwards. This was never described in literature before.

Although this is the first study investigating the influence of OSA on weight loss in bariatric surgery patients, the exact role of OSA in obesity, weight regain/insufficient weight loss, and the appearance of other related comorbidities such as type II diabetes and hypertension has not fully been investigated,

yet. Future research is needed in order to understand the exact physiology of OSA and associated comorbidities. The association between OSA and weight gain might change due to physical and anatomic changes after bariatric surgery. Additionally, as weight loss was only analyzed in the short terms (6 months and 1 year), results on the long term are interesting in future studies.

### Predictors for Insufficient EWL ( $\leq 50\%$ )

In multivariable logistic regression analysis, gender, age, preoperative BMI and AHI, type of surgery, and type II diabetes appeared to provide the best model prediction insufficient weight loss ( $\leq 50\%$  EWL). This model explains 21 % of  $\leq 50\%$  EWL, 1 year after bariatric surgery.

Five of these variables, including gender, age, preoperative BMI, type of surgery, and type II diabetes, are in agreement with literature [7, 8, 11, 12]. Although waist circumference was found to be a predictor in other studies, this variable gave no improvement to the multivariable model in present study. Perhaps, this variable could be added in a prediction model in other study populations or in combination with other variables.

This was the first study that included the AHI in the multivariable regression analysis. Since in the present population, preoperative P(S)G was performed in most patients and not only based on questionnaires and/or clinical parameters, the AHI can be regarded as a reliable predictor in the whole study population. Although adding this variable to the model gave improvement of the ROC-curve, the odds ratio was 0.992, showing a slightly protecting effect for  $\leq 50\%$  EWL. This might be the result, however, of predictors that are taken over by other characteristics than the AHI or the chosen definition for insufficient weight loss. By dichotomizing the outcome ( $\leq 50$  or  $> 50\%$  EWL), essential information is lost. It can be concluded that the statistical value of OSA in the multivariable predictive equation is weak and that the AHI was not the most prominent variable.

This study provided a non-validated prediction model explaining 20 % of  $\leq 50\%$  EWL, 1 year after bariatric surgery. This shows that 80 % of  $\leq 50\%$  EWL is explained by other factors. As Karmali et al. reported, the problem of insufficient weight loss is likely to be multifactorial, including medical, surgical, and physiological aspects [3]. Future research is required to reveal more predictive factors for insufficient weight loss. In order to provide better preoperative education and awareness, an optimal prediction model needs to be developed.

### Conclusion

A significant decreased %EWL is seen in OSA patients, especially in those with severe OSA, when compared to patients without OSA, 1 year after bariatric surgery. However, this effect seems to disappear after correcting for the variables

waist circumference, BMI, and age, which are correlated with OSA and have a known relationship with postsurgical weight loss. In addition, no difference was detected in mean BMI loss. Six variables including the AHI provided a good prediction model for insufficient weight loss i.e.,  $\leq 50\%$  EWL (AUC 0.771). Although the statistical value of the AHI was of little importance, the AHI was included in the model as it might have a more prominent role in other or larger cohorts. Therefore, it should be tested in larger (and long term) patient cohorts before its value as a predictor can be assessed. CPAP compliance during the relevant follow-up period should then be assessed as well. With current study results, it can be concluded that OSA itself has no important influence on weight loss after bariatric surgery.

**Conflicts of Interest** The authors declare that they have no competing interests.

**Compliance with Ethical Standards** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. As this was a retrospective study, formal national consent is not required.

**Informed Consent** Does not apply.

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