Obstructive sleep apnoea remission following bariatric surgery: lessons from the UK National Bariatric Surgical Registry

Abstract

Background: Obstructive sleep apnoea (OSA) is strongly associated with metabolic syndrome. Bariatric surgery is an effective available treatment for OSA; however, there has been limited research predicting which patients undergoing bariatric surgery will experience cure of OSA. This study aimed to determine preoperative predictors for OSA resolution following bariatric surgery using a national database.

Methods: The UK National Bariatric Surgery Registry (NBSR) was interrogated to identify all patients with OSA that underwent primary bariatric surgery between January 2009 and June 2017. Those with at least one follow-up recording post-operative OSA status were selected for further analysis. Demographic, pre- and post-operative outcomes were collected and analysed. Poisson multivariate regression was conducted to identify predictors of OSA remission.

Results: A total of 4015 bariatric cases were eligible for inclusion: 2,482 (61.8%) patients underwent LRYGB, 1,196 (29.8%) LSG and 337 (8.4%) LAGB. Overall, the mean excess weight loss % for the whole group was 61.2 (SD±27.2). OSA resolution was recorded in 2,377 (59.2%) patients. Following Poisson regression, procedure type affected OSA remission, with both LRYGB (RR 1.49 (confidence interval (CI) 1.25-1.78)) and LSG (1.46 (CI 1.22-1.75) being associated with approximately 50% increased likelihood of OSA remission compared to LAGB. Greater weight loss following intervention was associated with greater likelihood of OSA remission, while both greater age and greater preoperative BMI were associated with reduced likelihood of OSA remission ($p<0.001$).

Conclusion: This study demonstrated that metabolic surgery results in OSA remission in the majority of patients with obesity. Younger age, lower BMI pre-procedure, greater %EWL and the use of LSG or LRYGB positively predicted OSA remission.

Introduction

Bariatric surgery has proven benefits in reducing obesity-related co-morbidities and improving survival in patients with obesity[1, 2]. Obstructive sleep apnoea (OSA) is the most common sleep-related breathing disorder, for which obesity is a major risk factor[3]. Screening studies suggest OSA could exist in as much as 75% of the pre- population undergoing bariatric surgery[4-6]. Whilst the mechanistic relationships between obesity and OSA have yet to be fully elucidated, obesity is thought to contribute to OSA through fat deposition and local pressure-effect changes around the upper airways[7]. However studies suggest that OSA can be prevalent even in non-obese patients with type 2 diabetes[8, 9] and polycystic ovarian syndrome[10], indicating the additional involvement of non-adiposity related metabolic pathways.

Positive pressure ventilation instruments[11] are used to alleviate the symptoms of OSA, but do not treat the underlying cause. In selected patients, local maxillofacial surgical interventions to the upper airways can be effective [12]. Weight loss, however, is the mainstay of treatment for patients with obesity and OSA; and can also lead to improvements in associated obesity-related co-morbidities.

Bariatric surgery, which leads to dramatic and sustainable weight loss, has been shown to be an effective method of treatment of OSA [12] - a large cohort study from the Michigan Bariatric Surgical Collaborative recently demonstrated two-thirds of patients undergoing laparoscopic Roux-en-Y gastric bypass (LRYGB) or sleeve gastrectomy (LSG) experienced self-reported OSA remission[13]. There is however a relative paucity of high-quality outcome data on this subject; and the optimum bariatric procedure to treat OSA remains unclear [14].

The purpose of this study was to utilise a large national database (the prospectively collated United Kingdom National Bariatric Surgery Registry) to assess the

outcomes of bariatric surgery on the incidence of OSA remission; and to analyse the clinical and intervention-related predictors of OSA remission.

Methods

The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[14] guidance.

Study setting

Data from the UK National Bariatric Surgery Register (NBSR) was utilised for this study: this has been described previously[15]. Briefly, the NBSR is a prospectively collected nationwide registry of all bariatric surgical procedures undertaken in the United Kingdom and Ireland, comprising preoperative, operative and follow-up data.

Study population

Patients with a preoperative diagnosis of OSA who underwent primary bariatric surgery between January 2009 to May 2017 were included in the study. Of these, patients that did not have at least one follow-up visit in which OSA status was recorded, between 12- and 24 months post-surgery, were excluded. Where patients had more than one follow-up visit during this time frame, data from the most recent visit was utilised.

Data collection and outcomes

Data regarding preoperative demographic characteristics, presence of comorbidities (T2DM, liver disease, cardiovascular disease, gastro-oesophageal reflux disease (GORD), asthma, hypertension, dyslipidaemia, arthritis and depression) and treatment for comorbidities. Postoperative variables including length of follow-up, short-term postoperative outcomes, percent total weight loss and presence of OSA were extracted and analysed. Patients were considered to have OSA for the purpose of the study when they had a recorded diagnosis of OSA and were receiving treatment preoperatively or were diagnosed with OSA with complications. At follow-up, OSA remission was considered to

have occurred when OSA treatment had stopped and symptoms had been recorded as resolved. Patients were recorded as been diagnosed with type 2 diabetes or hypertension when they required ≥1 medications for those conditions. Patients reporting reflux symptoms or taking intermittent or daily gastrooesophageal reflux disease (GERD) medication were recorded as being diagnosed with GERD.

Statistical analysis

The primary outcome for this study was remission of sleep apnoea at follow-up 1-2 years post-bariatric surgery as defined by paucity of symptoms and discontinuation of OSA management. Percent weight loss (%WL) was calculated as percent of total weight lost using the following formula: % WL = 100 x (Follow up Weight – Initial Weight) / Initial Weight.

Percent excess weight loss (%EWL) was calculated based on an optimum body mass index (BMI) of 25kg/m^2, using the following formula: % EWL = 100 x (Follow up BMI – Initial BMI) / (Initial BMI – 25).

Comparison of baseline factors and outcomes by procedure was initially carried out by analysis of variance or chi-square tests as appropriate. Further adjusted comparison of factors predicting OSA remission following metabolic surgery were made using Poisson regression (PROC GENMOD, SAS version 9.4). For procedure type, LAGB was chosen as the reference category. The model outcome was parameterised as being 'OSA remission', with an offset included to account for variable follow-up time. To account for clustering of effect, hospital was placed as a random effect within the model. Baseline factors used for adjustment were age, gender, initial BMI, smoking, number of co-morbidities and dyslipidemia.

Results

From 10,253 patients with documented OSA who underwent primary bariatric surgery during the time period of interest, 4015 (39.4%) had suitable follow-up for inclusion (Figure 1).

The mean age of patients was 48.7 years (SD ±9.7 years) with a slight female preponderance (57.9%) and the majority of patients (90.9%) were Caucasian (Table 1). The mean preoperative body mass index (BMI) of these patients was 51.1 kg/m^2 (SD ±8.3 kg/m^2) with a mean preoperative weight of 145.8 kg (SD±28.2kg). Just over half (53.6%) of patients had 2 or more co-morbidities, and most were recorded as non-smokers or ex-smokers (90.7%). In terms of surgical procedures, 2,482 (61.8%) patients underwent LRYGB, 1,196 (29.8%) of patients had LSG and 337 (8.4%) received LAGB.

Patients were followed-up for a mean of 471 days (Table 2). At follow-up, patients had a mean BMI of 35.5kg/m^2 (SD±8.5 kg/m^2) and a mean weight of 101.4 kg (SD±28.5 kg). Mean total weight loss was recorded as 44.5kg (SD±25.2kg). Overall, the mean excess weight loss % for the whole group was 61.2(SD±27.2). Operative procedure was associated with differences in %EWL: patients who underwent LRYGB had the greatest excess weight loss (67.8%), followed by those who had LSG (55.4%) whilst patients who had a LAGB inserted lost on average a third of their excess weight (33.2%).

OSA resolution was recorded in 2,377 (59.2%) patients. Of these, the highest resolution was seen in the LRYGB group (64.5%) as opposed to 56.1% in the LSG group and 31.2% of those who underwent LAGB. Following adjustment, procedure type predicted OSA remission ($p<0.001$), with both LRYGB and LSG being associated with approximately 50% increased likelihood of OSA remission (Table 3). Increased post-operative weight loss was additionally associated with a greater

likelihood of OSA remission, while both increasing age and increasing preoperative BMI were associated with a reduced likelihood of OSA remission ($p<0.001$). Presence of dyslipidaemia also associated with small but statistically significant increased likelihood of resolution ($p<0.001$). Gender, smoking and comorbidities were not predictive of OSA outcome.

Discussion

This study represents the largest series investigating preoperative predictors of OSA resolution following bariatric surgery and demonstrates a number of important findings. We observed that bariatric surgery was associated with remission of OSA in approximately 60% of patients- a figure consistent with that obtained in the Michigan Bariatric Surgery Collaborative study [13]. Younger age, lower preoperative BMI, and higher weight loss were all associated with an increased likelihood of OSA remission in our study. Whilst the Michigan study [13] found gender and co-morbidity influenced OSA remission outcomes, those findings were not replicated in this current study. There are notable differences in ethnicity distribution between this study and the Michigan study, which are known to significantly influence the interaction between obesity and OSA[16]. It should be noted that in our study average age of the patients was 49 which is considerably higher than the average age of worldwide bariatric surgery patients[17]. Given older patients tend to have higher BMI and have reduced weight loss after bariatric surgery[18], it may be that our study underestimates the positive effect of surgery by masking the potential positive effects for surgery on younger patients.

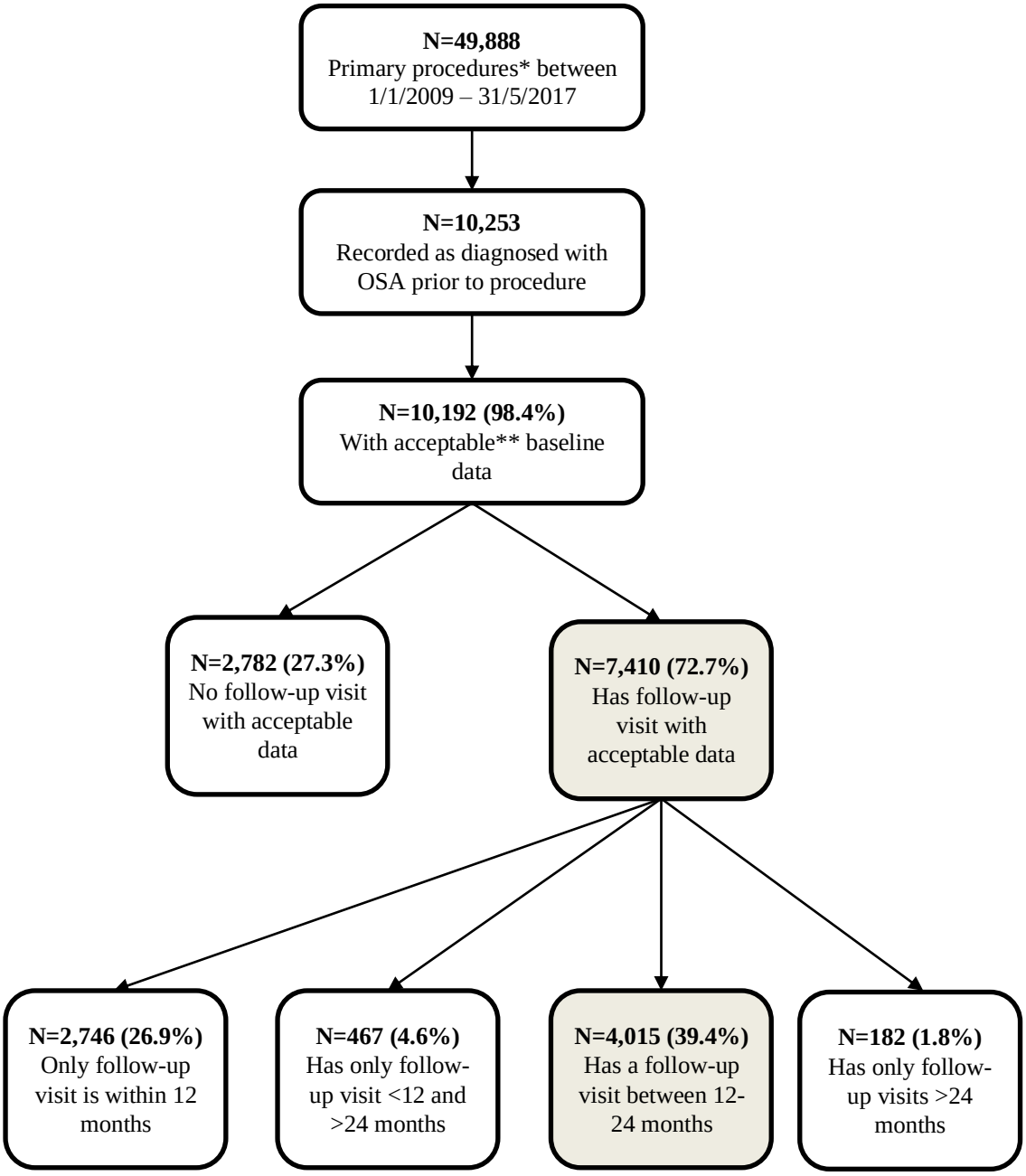
With regard to surgical intervention, LSG and LRYGB were associated with increased probability of OSA remission compared to LAGB. Interestingly this effect persisted even after adjustment for the differential weight losses associated with the three procedures. Although weight loss has been known to improve and in some cases resolve OSA [19], a number of metabolic pathways have been implicated in OSA pathophysiology that are independent of the weight and BMI such as improved glycaemic control and reduced systemic inflammation[20]. For example a recent study demonstrated that polysomnography analysis applied only 3 week post-metabolic surgery showed reduced apnoeic-hypoxic events together with significant neurohormonal changes, before significant weight loss [21]. Our findings appear to support the concept of bariatric surgery deriving OSA remission

through both weight-loss and weight-independent pathways, and that these weight-independent, metabolic effects appear more pronounced following RYGB and LSG as compared to LABG.

We accept that our study has a number of limitations that require further explanation. The NBSR registry uses a binary definition of OSA resolution and does not record any physiological measures, meaning that the actual beneficial effect of surgery may be underestimated (as a patient that requires lower positive pressure support would be recorded as still requiring therapy). We also accept that the follow up rate was low (with only 39% having a follow-up visit that made them suitable for inclusion), though this follow up rate is comparable to some other Registry studies[13, 22], although the Scandinavian registries with their linkage to national identification numbers demonstrate more complete follow-up[23]. With regard to the comparison of the individual operative procedures, this was not a randomised controlled trial and hence there were significant disparities in the size, demographic and clinical characteristics of the cohorts of patient undergoing AGB, SG and RYGB (though these differences were accounted for in our statistical analysis). Finally, the study was not able to explore the impact of newer metabolic procedures, such as one-anastomosis gastric bypass due to the small number of reported procedures in the NBSR at the timepoint of analysis. Nonetheless, we do feel that the large size of the cohort adds considerable weight to our findings.

In summary, this study demonstrates that based on "real world data" bariatric surgery results in OSA remission in the majority of patients with morbid obesity. A number of predictors of OSA remission identified in this study may be used to guide the preoperative discussion process including younger age, lower BMI pre-procedure, greater excess weight loss and the use of LSG or LRYGB. Greater understanding of the phenotypes of patients with obesity and OSA may assist a more personalised pathway and trigger earlier discussion of the need for metabolic surgical intervention.

Figure 1. Case selection for study patients within NBSR



* - Gastric Band, Roux en Y gastric bypass, Sleeve gastrectomy
** - Must have non-zero Age (range 13-81), Initial Weight between 70-400kg, Height 1-2m and OSA status recorded.

Table 1: Baseline Data

	All (n=4,015)	LAGB (n=337)	LSG (n=1,196)	RYGB (n=2,482)	p-value**
Means (SD)					
Mean Age	48.7 (9.7)	49.4 (9.8)	49.0 (9.7)	48.5 (9.7)	0.15
Mean Initial Weight	145.8 (28.2)	137.9 (25.0)	153.1 (31.0)	143.4 (26.4)	<0.001
Mean Initial BMI	51.1 (8.3)	48.7 (7.2)	53.3 (9.3)	50.4 (7.7)	<0.001
Mean Co-morbidities	1.6 (1.0)	1.4 (1.0)	1.6 (1.0)	1.7 (1.0)	<0.001
N (%)					
Male Gender	1,690 (42.1)	134 (39.8)	561 (46.9)	995 (40.1)	<0.001
Ethnicity*					
- Caucasian	3,502 (90.9)	305 (93.9)	1,013 (87.2)	2,184 (92.3)	<0.001
- Non-Caucasian	351 (9.1)	20 (6.2)	149 (12.8)	182 (7.7)	
Smoking*					
- Never	2,021 (52.4)	167 (51.1)	671 (58.3)	1,184 (49.7)	<0.001
- Ex	1,478 (38.3)	130 (39.8)	374 (32.5)	974 (40.9)	
- Current	359 (9.3)	30 (9.2)	107 (9.3)	222 (9.3)	
Co-morbidities					
- 0	616 (15.3)	74 (22.0)	181 (15.1)	361 (14.5)	<0.001
- 1	1,247 (31.1)	124 (36.8)	390 (32.6)	733 (29.5)	
- 2	1,165 (29.0)	76 (22.6)	333 (27.8)	756 (30.5)	
- 3 or more	987 (24.6)	63 (18.7)	292 (24.4)	632 (25.5)	
Dyslipidemia*					
- No	2,508 (62.6)	252 (74.8)	730 (61.1)	1,526 (61.7)	<0.001
- Yes	1,498 (37.4)	85 (25.2)	464 (38.9)	949 (38.3)	

* Expressed among those with a recording in each category. Missing data for the following categories was: n=157 (3.9%) had no smoking data record, n=162 (4.0%) had no ethnicity recorded, n=9 (0.2%) had missing data for Dyslipidemia.

** P-value for tests of heterogeneity between procedure type (ANOVA or chi-square test)

Table 2: Follow-Up Data

	All (n=4,015)	LAGB (n=337)	LSG (n=1,196)	RYGB (n=2,483)	p-value*
Means (SD)					
Mean Follow-up (days)	471 (100)	469 (91)	470 (99)	472 (102)	0.77
Mean BMI (kg/m^2)	35.5 (8.5)	41.2 (7.4)	38.0 (7.5)	33.6 (8.5)	<0.001
Mean Weight (kg)	101.4 (28.5)	116.6 (24.2)	109.1 (24.7)	95.6 (29.1)	<0.001
Mean Weight Loss (kg)	-44.5 (25.2)	-21.3 (13.6)	-43.9 (19.9)	-47.7 (27.0)	<0.001
Mean Excess weight loss %	61.2 (27.2)	33.2 (20.8)	55.4 (20.3)	67.8 (27.8)	<0.001
N (%)					
OSA Resolved	2,377 (59.2)	105 (31.2)	670 (56.1)	1,602 (64.5)	<0.001

* P-value for tests of heterogeneity between procedure type (ANOVA or chi-square test)

Table 3: Adjusted Relative Risks for OSA Resolution (n=4,015)

	N	% with OSA Resolution	Unadjusted RR (95% CI)	Mutually Adjusted RR (95% CI)
Operation Type				
- LAGB	337	31.2	1	1
- RYGB	2482	64.5	1.99 (1.64-2.42)	1.49 (1.25-1.78)
- LSG	1196	56.0	1.76 (1.47-2.11)	1.46 (1.22-1.75)
p-value*			<0.001	<0.001
Age (years)				
- 17 to 39	700	64.1	1	1
- 40 to 49	1330	60.2	0.94 (0.86-1.02)	0.94 (0.87-1.03)
- 50 to 59	1444	59.4	0.91 (0.84-0.99)	0.90 (0.84-0.98)
- 60 +	541	49.9	0.78 (0.70-0.86)	0.78 (0.71-0.86)
p-value*			<0.001	<0.001
Gender				
- Female	2325	60.1	1	1
- Male	1690	58.0	0.95 (0.89-1.02)	0.95 (0.90-1.00)
p-value*			0.14	0.07
Initial BMI (kg/m^2)				
- 45 or less	897	60.3	1	1
- 45 to 50	1056	62.9	1.00 (0.93-1.08)	1.01 (0.93-1.09)
- 50 to 55	945	58.2	0.93 (0.85-1.02)	0.96 (0.88-1.04)
- 55 to 60	596	58.6	0.89 (0.79-1.01)	0.93 (0.84-1.03)
- 60 or more	521	52.4	0.80 (0.70-0.92)	0.84 (0.73-0.96)
p-value*			<0.001	<0.001
Excess Weight Loss (%)				
- 25% or less	227	28.6	1	1
- 25 to 50%	945	48.5	1.74 (1.32-2.29)	1.52 (1.21-1.92)
- 50 to 75%	1792	61.3	2.22 (1.64-3.01)	1.84 (1.44-2.36)
- 75 to 100%	908	70.5	2.52 (1.79-3.55)	2.01 (1.52-2.65)
- 100% or more	143	80.4	2.88 (2.06-4.03)	2.22 (1.69-2.92)
p-value*			<0.001	<0.001
Smoking*				
- Never	2021	58.0	1	1
- Ex vs Never	1478	59.7	0.99 (0.92-1.07)	0.98 (0.91-1.05)
- Current vs Never	225	62.7	1.07 (0.96-1.19)	1.02 (0.92-1.12)
p-value*			0.59	0.83
Co-Morbidities				
- 0	616	60.9	1	1
- 1	1247	58.4	0.95 (0.87-1.04)	0.96 (0.88-1.04)
- 2	1165	59.4	0.98 (0.90-1.07)	0.98 (0.90-1.06)
- 3 or more	987	59.0	0.94 (0.85-1.04)	0.94 (0.86-1.03)
p-value*			0.59	0.59
Dyslipidemia**				
- No	2508	57.5	1	1
- Yes	1498	62.2	1.06 (1.00-1.12)	1.11 (1.05-1.18)
p-value*			0.04	<0.001

* p-values test for heterogeneity or trend as appropriate
** Note that a missing/not recorded category was fitted for smoking (n=157) and dyslipidemia (n=9)

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