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Obstructive Sleep Apnea Before and 10 Years After Bariatric Surgery

Master's thesis in Profesjonsstudiet i Medisin

Supervisor: Kjetil Roth

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Abstract English

Background: Bariatric surgery has been observed to have positive effects on obstructive sleep apnea (OSA) on a short-term basis. As bariatric surgery has been shown to be an effective way to maintain weight loss for patients with obesity, it is important to know the long-term effect it has on common comorbidities associated with obesity.

Objective: To explore if bariatric surgery has a long-term positive effect on OSA, and if there is a correlation between decrease in BMI and ODI.

Material and Methods: Patients with obesity that had bariatric surgery as primary treatment, that were assessed for OSA before surgery and reassessed 10-15 years later.

Results: Of 61 patients with OSA before surgery, 15 (54%) men and 21 (64%) women were treated with CPAP. Mean ODI before surgery was 27 [0-63] for men and 21 [0-60] for women. Of 32 patients in the follow up 10-15 years after surgery, the mean ODI had decreased from 20 [0-51] before surgery to 7 [0-24] at the follow up. The mean BMI had also decreased from 45 [32-57] before surgery to 34 [23-44] at the follow up. 16 of the 32 (50%) patients had an ODI of 15 or higher before surgery, but only 1 (3%) patient had an ODI of 15 or higher after surgery. At the follow up there was also only 1 (3%) patient still in need of CPAP treatment. There was no correlation between decrease in ODI and decrease in BMI.

Conclusion: At the follow up, 10-15 years after surgery, only 1 patient was still in need of CPAP treatment, and out of 32 patients, only 5 were still diagnosed with OSA. There was no correlation between decrease in ODI and BMI.

Abstract Norsk

Bakgrunn: Fedmekirurgi har blitt observert med positiv effekt på obstruktiv søvnapne i kortsiktige studier. Ettersom man har vist at fedmekirurgi er en effektiv måte å opprettholde et vekttap for pasienter med fedme er det viktig å kjenne til langtidseffektene operasjonen kan ha på vanlige komorbiditeter assosiert med fedme.

Objektiv: Å undersøke om fedmekirurgi har en positiv effekt på obstruktiv søvnapne på lengre sikt, og om det er korrelasjon mellom nedgang i BMI og ODI.

Material og metode: Pasienter med fedme som ble behandlet med fedmekirurgi som primærbehandling, og som ble undersøkt for obstruktiv søvnapne før kirurgi og på nytt 10-15 år etter operasjonen.

Resultater: Av 61 pasienter med obstruktiv søvnapne før de ble operert var det 15 (54%) menn og 21 (64%) kvinner som ble behandlet med CPAP. Gjennomsnittlig ODI før kirurgi var 27 [0-63] for menn og 21 [0-60] for kvinner. Av 32 pasienter som ble vurdert før operasjonen og på nytt etter 10-15 år hadde gjennomsnittlig ODI sunket fra 20 [0-51] før kirurgi til 7 [0-24] etter 10 år. Gjennomsnittlig BMI hadde også sunket fra 45 [32-57] før kirurgi til 34 [23-44] ved oppfølging. 16 av 32 (50%) pasienter hadde en ODI på 15 eller høyere før operasjon, og etter operasjon hadde kun 1 (3%) pasient fortsatt en ODI på over 15. Det var også kun 1 (3%) pasient som fortsatt ble behandlet med CPAP ved oppfølging. Vi fant ingen korrelasjon mellom reduksjon i BMI og reduksjon i ODI.

Konklusjon: Ved oppfølging, 10-15 år etter operasjonen, ble kun 1 pasient fortsatt behandlet med CPAP for sin OSA. Av 32 pasienter med OSA før operasjon var det kun 5 som fortsatt hadde diagnosen. Det var ingen korrelasjon mellom nedgang i ODI og BMI.

Introduction

Obesity is a worldwide disease affecting both children and adults. It is also a disease associated with increased risks of developing several comorbidities, for example hypertension, dyslipidemia, cardiovascular disease and obstructive sleep apnea (OSA). (1)

OSA is a disease characterized by multiple apneas or hypopneas during sleep, caused by a partial or complete collapse of the upper airways. This results in intermittent hypoxia and a fragmentation of sleep. (2) OSA can cause excessive daytime sleepiness, higher risk of hypertension, cardiovascular disease, and neurocognitive impairment. (3) Because of the increase in daytime sleepiness there is also an association with higher risks of accidents, especially associated with motor vehicles, and a poorer quality of life. (4)

OSA is determined and graded using apnea-hypopnea index (AHI) or oxygen desaturation index (ODI). The gold standard for diagnosis of OSA is polysomnography in a sleep laboratory, but it can also be diagnosed by monitoring the oxygen saturation in the blood during sleep using a pulse oximeter. The severity of OSA is graded from mild to severe.

The current treatment available for OSA is mainly Continuous Positive Airway Pressure (CPAP) treatment which prevents the airways from collapsing during sleep. (5) CPAP does not cure OSA, but it is effective in treating the symptoms. (6) CPAP is considered the default treatment for OSA, but weight loss has also been shown to have great positive effect. (7) CPAP also has some side effects such as sleep interruption, skin irritation, dryness of the airways, claustrophobia, and congested airways. Several patients also discontinue their CPAP treatment. (4, 8)

OSA is a disease strongly associated with obesity (9). Bariatric surgery has been proven as an effective method to obtain and maintain weight loss in patients with obesity (10, 11), and has also shown to be effective in reducing the severity of sleep apnea or even resolving it after surgery. (12-14) However this is mostly documented in studies with short follow up-time, usually 1-2 years at most. (12)

There has also been performed studies showing the correlation between weight and AHI, where one study found that a 10% increase in body weight increased the patients AHI with 32% [20-45%], and that a weight reduction of 10% gave a 26% [18%-34%] reduction in AHI. (15) Another study found that the odds ratio for every point increased in BMI was a 1,14 [1,10-1,19] increase in AHI. (16) This study also found that male gender, increasing age,

hyperlipidemia, and an increase in waist-hip-ratio were significantly associated with higher AHI.

In the present study we used data from the BAROBS study in Norway with a minimum of 10 year follow up of patients who have undergone bariatric surgery in the period 2003-2009. The patients included in the BAROBS study were operated by Roux-en-Y gastric bypass (RYGB) in Ålesund hospital, Namsos hospital, and St. Olavs Hospital.

The aims of this study were to explore if bariatric surgery and sustained weight loss improved the patients OSA in long-time follow up. We also wanted to verify the correlation between the degree of obesity and the severity of OSA, and if weight loss correlated with improvement of OSA measured by ODI.

Material and Methods

This article is based on patients from the BAROBS study conducted at St. Olavs Hospital in Trondheim, Norway. The study is a retrospective analysis of prospectively collected data from patients that underwent RYGB as a primary treatment for morbid obesity. The patients underwent RYGB between 2003 and 2009. We included patients operated at St. Olavs Hospital and Aalesund hospital. The follow up of the patients happened between 2018 and 2020, 10-15 years after surgery. The study is approved by the Regional Ethical Committee (REK).

Between 2003 and 2009 a total of 597 patients underwent RYGB at St. Olavs hospital or Ålesund hospital. 403 of these patients were included in the BAROBS study. Before surgery the patients were assessed for OSA, either previously diagnosed or by doing a nightly pulse oximetry at home to provide the ODI-values. The diagnosis was based on their medical history and the results of the pulse oximetry, where $ODI < 5$ is considered normal, 5-15 is mild, 15-30 is moderate, and $ODI > 30$ is considered severe OSA. 61 of the patients had a documented OSA on pulse oximetry or a previous diagnosis of OSA and was included in this study. 32 patients redid the pulse oximetry at the follow up 10-15 years after surgery.

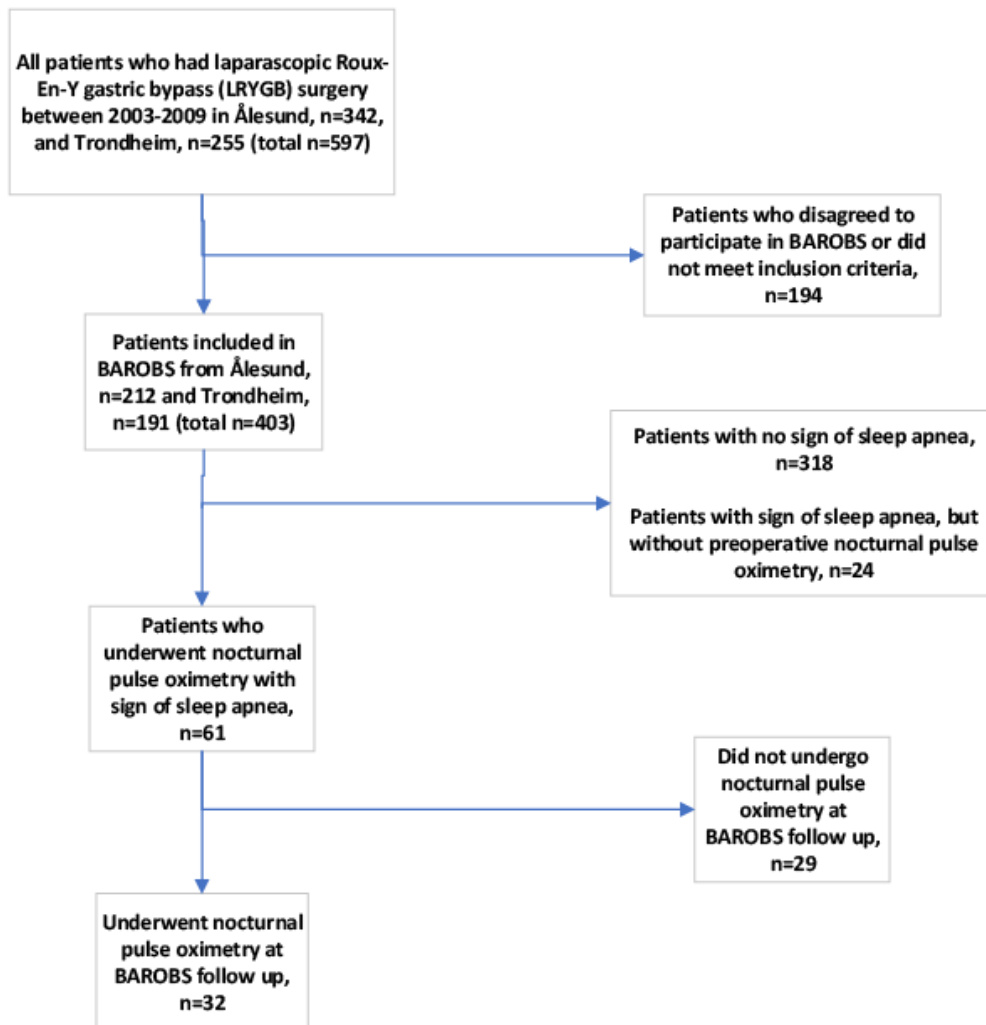


Figure 1: Flowchart showing patients included in study.

The data used in this article originates from data collected for the BAROBS study and from manually going through the included patients' medical journals. The data is stored anonymously in a dataset.

We utilized SPSS to analyze the data. The continuous variables that were normally distributed were analyzed with independent t-test, and the variable that was not normally distributed was analyzed using the explore-function in SPSS. This gave us the median and the interquartile range. To find the p-value we used U-Whitney Mann-test. The categorical values were analyzed by using chi-square test. We also created scatter plots and used linear regression to observe a potential correlation.

Results

Baseline Characteristics of 61 Patients with Sleep Apnea before Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) surgery

	Men n=28 (46%)	Women n=33 (54%)	
Continuous variables (normally distributed)	Mean [95% CI]	Mean [95% CI]	p-value¹
Weight (kg)	144 [98-190]	123 [85-161]	<0,001
Height (cm)	180 [165-194]	165 [153-177]	<0,001
BMI ² (kg/m ²)	45 [32-57]	45 [33-58]	0,8
Age (year)	45 [27-63]	43 [26-60]	0,5
ODI ³ (event/hour)	27 [0-63]	21 [0-60]	0,2
Lowest oxygen saturation during the night (%)	75 [59-91] * ⁴	76 [49-103] * ⁵	0,8
Epworth (/24)	10 [1-20] * ⁶	11,0 [0-26] * ⁷	0,8
Continous variables (not normally distributed)	Median [IQR]⁸	Median [IQR]	p-value⁹
Percentage of the night with saturation below 90% (%)	11 [15] * ¹⁰	7 [13] * ¹¹	0,1
Categorical variables	N¹² (%)	N (%)	p-value¹³
FEV1 ¹⁴ <80% of expected value	Yes: 10 (42) * ¹⁵ No: 14 (58)	Yes: 6 (20) * ¹⁶ No: 24 (80)	0,08
OSAS ¹⁷ treated with CPAP	Yes: 15 (54) No: 13 (46)	Yes: 21 (64) No: 12 (36)	0,4
Asthma	Yes: 3 (13) * ¹⁸ No: 21 (87)	Yes: 4 (13) * ¹⁹ No: 27 (87)	0,7
Smoking	Yes ²⁰ : 18 (64) No ²¹ : 10 (36)	Yes: 20 (62) * ²² No: 12 (38)	0,9
Hypertension	Yes: 14 (50) No: 14 (50)	Yes: 6 (18) No: 27 (82)	0,01
Diabetes M type 2	Yes: 8 (29) No: 20 (71)	Yes: 9 (27) No: 24 (73)	0,3
COPD	Yes: 0 (0) * ²³ No: 25 (100)	Yes: 0 (0) * ²⁴ No: 30 (100)	NS
Hyperlipidemia	Yes: 8 (29) No: 20 (71)	Yes: 2 (6) No: 31 (94)	0,02

¹p-value for t-test, ²Body Mass Index, ³Oxygen desaturation index, one event is a 4% fall in saturation, ⁴7 missing, ⁵10 missing, ⁶10 missing, ⁷19 missing, ⁸Interquartil range, ⁹P-value for Mann-Whitney test, ¹⁰3 missing, ¹¹4 missing, ¹²N equals number of patients who has the condition, ¹³P-value for chi-square test, ¹⁴Forced expiratory volume, ¹⁵4 missing, ¹⁶3 missing, ¹⁷Obstructive sleep apnea syndrome, ¹⁸4 missing, ¹⁹2 missing, ²⁰Currently smoker or in the past, ²¹Has never smoked, ²²1 missing, ²³3 missing, ²⁴3 missing

Table 1 Baseline Characteristics of 61 patients preoperatively

The study population of 61 consists of 28 (46%) men and 33 (54%) women, the average age at surgery was 45 [32-57] amongst the men and 43 [26-60] amongst the women. The mean BMI for men was 45 [32-57] and 45 [33-58] for women. All 61 patients had been diagnosed with OSA before surgery, and 15 (54%) of the men and 21 (64%) of the women were treated with CPAP before they underwent surgery. The mean ODI for men was 27 [0-63] and 21 [0-

60] for the women. 10 (42%) of the men and 6 (20%) of the women had reduced lung function showed with FEV1<80% of expected value. 18 (64%) of men and 20 (62%) of women are also smokers. 14 (50%) men and 6 (18%) (p=0,01) women have hypertension, which is a significant difference between the genders. There are also more men, 8 (29%), than women, 2 (6%) (p=0,02), with hyperlipidemia. None of the included patients had COPD, but 3 (13%) of men and 4 (13%) (NS) of women had asthma. Apart from hypertension and hyperlipidemia, none of the findings between men and women were significant.

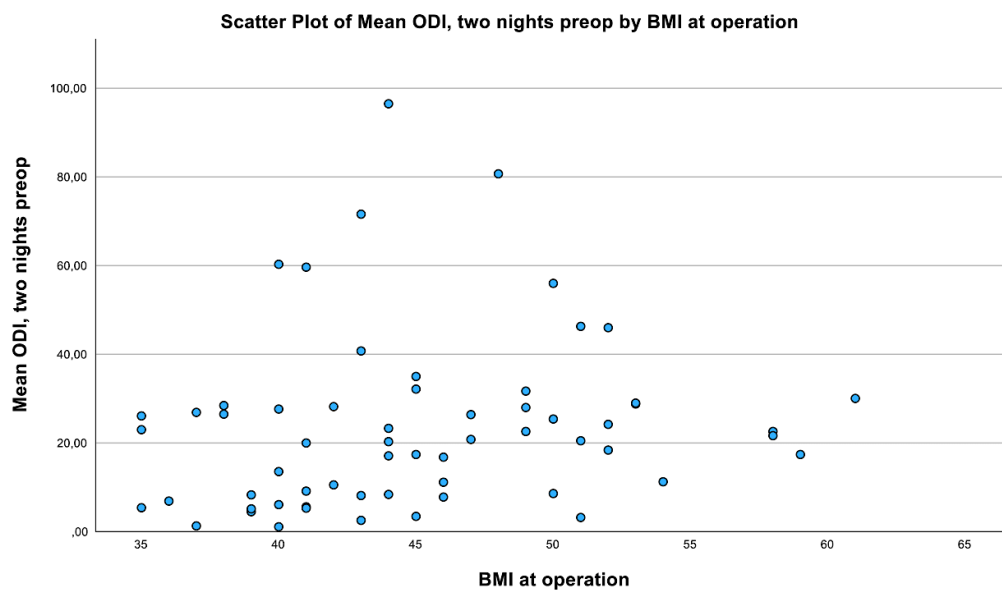


Figure 2 Scatter plot showing mean ODI and BMI preoperatively for 61 patients.

Fig.2 shows a scatter plot with mean ODI on the y-axis and BMI before surgery on the x-axis, to show a potential correlation between preoperative ODI and BMI. This shows no correlation. Linear regression which did not show correlation between the BMI and ODI in this population.

Comparison of values preoperatively and at BAROBS-follow up minimum 10 years after surgery in 32 patients.

	Preoperatively N=32		BAROBS-follow up (minimum 10 years after surgery) N=32	
Continuous variables¹	Mean [95% CI]		Mean [95% CI]	p-value²
Weight (kg)	130 [87-173]		97 [62-132]	<0,001
BMI ³ (kg/m ²)	45 [32-57]		34 [23-44]	<0,001
ODI ⁴ (event/hour)	20 [0-51]		7 [0-24]	<0,001
Lowest oxygen saturation during sleep (%)	73 [50-97] * ⁵		80 [58-102]	<0,001
Epworth (/24)	12 [0-23] * ⁶		8 [3-14] * ⁷	<0,001
Continuous variables⁸	Median [IQR⁹]	p-value¹⁰	Median [IQR]	p-value
Time spent with oxygen saturation under 90% (%)	10 [17] * ¹¹	0,03	1 [17] * ¹²	0,2
Categorical variables	N (%)		N (%)	p-value¹³
FEV1 ¹⁴ <80%	11 (37) * ¹⁵		10 (33) * ¹⁶	0,8
FEV1 >80%	19 (63)		20 (67)	
ODI ≥ 15 ¹⁷	16 (50)		1 (3)	<0,001
OSAS ¹⁸	Yes: 31 (100) No: (0) * ¹⁹		Yes: 5 (16) No: 26 (84) * ²⁰	<0,001
Patients treated with CPAP ²¹	24 (77) * ²²		1 (3) * ²³	<0,001

¹Variables with normal distribution, ²Pvalue from t-test, ³Body mass index, ⁴Oxygen desaturation index (events with 4% fall in oxygen saturation), ⁵5 missing, ⁶13 missing, ⁷24 missing, ⁸Variables that are not normally distributed, ⁹Interquartile range, ¹⁰P-value from U-Whitney Mann-test, ¹¹2 missing, ¹²missing, ¹³P-value from Chi-square test, ¹⁴Forced expiration volume during 1 second, patients with <80% of expected value, ¹⁵2 missing, ¹⁶2 missing, ¹⁷Patients with an ODI of 15 or higher, ¹⁸Obstructive sleep apnea syndrome, ¹⁹1 missing, ²⁰1 missing, ²¹Continuous Positive Airway Pressure, ²²1 missing, ²³1 missing

Table 2 Table comparing preoperative values and the same values at BAROBS follow up 10-15 years later in 32 patients.

Table 2 shows a comparison of measurements done before surgery and at the follow up, 10-15 years later in 32 patients. The mean weight has decreased from 130 [87-173] to 97 [62-132] ($p < 0,001$), and the mean BMI has decreased from 45 [32-57] to 34 [23-44] ($p < 0,001$). The mean ODI has also decreased from 20 [0-51] to 7 [0-24] ($p < 0,001$). The table also shows that before surgery, 16 (50%) of the patients had an ODI of 15 or higher, and at the follow up only 1 (3%) ($p < 0,001$) patient had an ODI of 15 or higher. All the patients were diagnosed with OSA before surgery, and at the follow up only 5 (16%) ($p < 0,001$) patients were still diagnosed with OSA. It is also significant that only 1 (3%) patient was treated with CPAP at the follow up, compared to the 24 (77%) ($p < 0,001$) before surgery. The table also shows that before surgery the median time spent with oxygen saturation below 90% was 10% [IQR 17] of the night, whereas at the follow up the median was only 1% [IQR 17] (NS). The minimum

oxygen saturation had also increased from 73% [50-97] before surgery, to 80% [58-102] ($p < 0,001$) at the follow up. The lung function is similar before surgery and at the follow up, with 11 (37%) with FEV1 under 80% of the expected value before surgery, and 10 (33%) (NS) at the follow up.

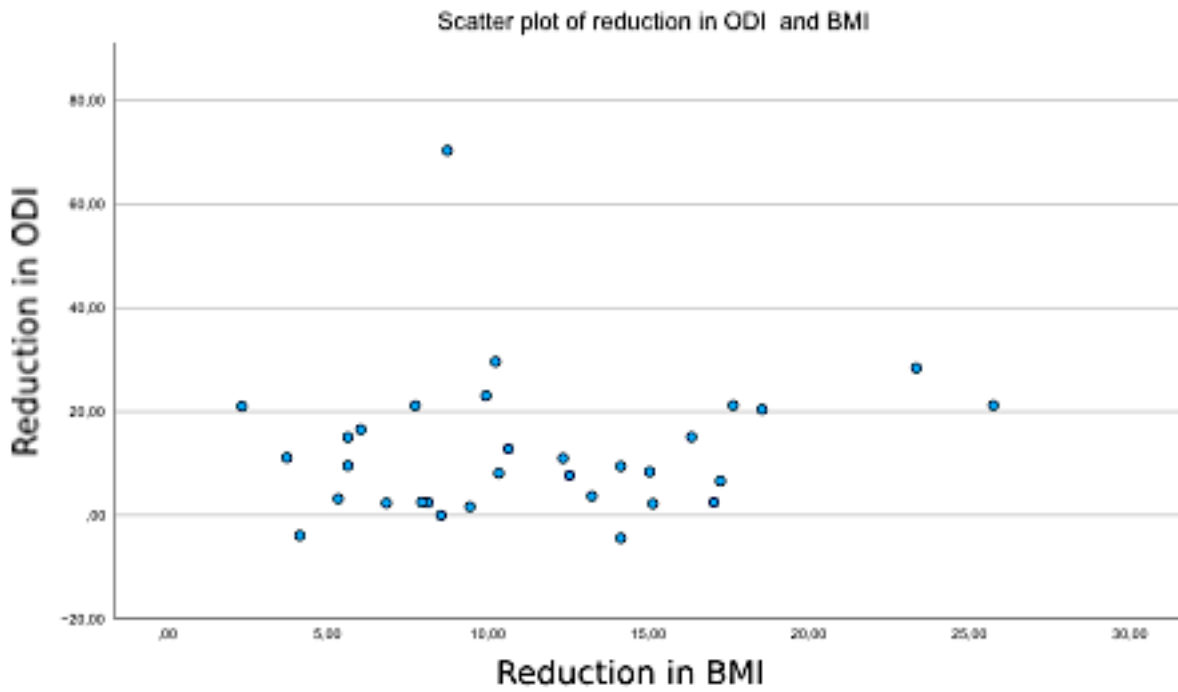


Figure 3 Scatter plot showing the difference in ODI before surgery and at follow up, and the difference in BMI before surgery and at the follow up.

Fig.3 shows a scatter plot with the reduction in ODI before surgery and after the follow up and the reduction in BMI before surgery and after the follow up. Most patients improved their ODI with 0-30 desaturations per hour, and decreased their BMI with 5-15 units, but there was no correlation between amount of weight lost and improvement of ODI. In addition, a linear regression performed on the reduction in ODI and the reduction in BMI did not show any correlation.

Discussion

This study aimed to show how bariatric surgery can affect sleep apnea in patients on a long-term basis. From table 2 we can see that out of the 32 (100%) patients included with OSA before surgery, only 5 (16%) of the patients were still diagnosed at the follow up, and only 1 (3%) patient was still treated with CPAP for their OSA. We did not find a correlation between the reduction in ODI and the reduction in BMI at the follow up.

16 (50%) patients had an ODI of 15 or higher before surgery, which means they had a moderate to severe OSA. Out of the 32, only 1 (3%) of the patients had an ODI of 15 or more at the follow up. Even though the bariatric surgery did not resolve OSA for all patients, 26 (81%) of the patients did not have OSA at the follow up appointment 10-15 years after the surgery, and only 1 (3%) patient had an $ODI \geq 15$. Only 1 (3%) patient needed CPAP treatment at the follow up. This is important as it shows the significant positive effects bariatric surgery has had for the patients, including the weight loss. This also shows that the effect on OSA is not limited to the first couple of years after surgery, it seems to persist. This is interesting considering most studies done on this subject has a short follow-up time.

De Raaff et.al (13) found in 2016 that 75% of the patients included with $AHI \geq 15$ achieved a postoperative $AHI < 15$, but 25% of patients still had an $AHI \geq 15$. They discovered age ≥ 50 years, excess weight loss $< 60\%$, hypertension, and preoperative $AHI \geq 30$ to be predictive factors of the persistence of OSA after surgery. This study had a follow up of 8,6 months (4,8 standard deviation), which is a lot shorter than our study, but it is interesting how different factors affect the results. There was only 1 out of the 32 patients that still had a moderate to severe OSA in our population, but it could be interesting to further investigate if they had any predictive factors for persistent OSA.

Table 2 also shows that even though OSA was not resolved in all patients the overall condition of their sleep seemed to have improved. The minimum oxygen saturation has increased from 70% to 80% during the night, which leads to less nocturnal hypoxemia. This is also found in a meta-analysis from 2018, where they found that the mean oxygen saturation during night increased by 1,36 [0,72-2,00] and the minimum oxygen saturation increased by 1,08 [0,68-1,49] after surgery. (17)

At both the preoperative assessment and the follow up-appointment the patients were assessed with Epworth's sleepiness scale. Several patients did not fill this out neither at the preoperative assessment, nor at the follow up-appointment, but it is also interesting that the decrease is from 12 [0-23] to 8 [3-14]. This is the variable with the highest number of missing, so it might not be representative for the study population.

One of the strengths of this study is the long follow up time, as this gives us the opportunity to show that the sleep apnea is resolved, or greatly improved, 10-15 years after surgery. And it also shows that in the cases that the sleep apnea is not resolved, it is improved. This can give a good indication for how bariatric surgery affects patients and comorbidities such as OSA in

the long term. Another strength is that all patients were assessed before surgery if they had OSA or not, so it was possible to look at a big population and see how many had OSA before surgery. Another strength is also the documentation of ODI at the follow up, even if the patient no longer had sleep apnea.

One weakness of this study is the differing practices regarding preoperative data collection between hospitals. In addition to the differing practices at the different hospitals, the practices at the hospitals also seemed to change between 2003 and 2009, since before 2007 the paper journals were seen as the legal documentation and there are varying degrees of digitalization of these journals. Since the preoperative data gathering was not standardized this has led to us missing documentation for several of the patients. Another weakness is also that this is an observational study, which can make it harder to avoid bias and confounding.

The small study population is also a big weakness of this study, especially since we only had documentation both preoperatively and at follow up to evaluate 32 patients with previously diagnosed sleep apnea. With such a small population it is challenging to utilize the findings to say anything definitive about the general population. Another weakness is also that several patients who were assumed to have sleep apnea prior to the preoperative assessment did not undergo the nightly pulse oximetry due to them already being diagnosed, which meant we did not have documentation of their condition with ODI. This might have affected which patients were included in this study, since the patients with prior diagnoses could have been more bothered by their condition than those who were diagnosed at the preoperative assessment.

There was a lot of data missing in the dataset from the study and in the patients' journals. This might stem from the fact that the data was collected from two different hospitals. Since the documentation process both before surgery and at the follow up was not standardized between hospitals this has led to us only having 32 patients with enough documentation to compare before and after surgery. On the other hand, we had good enough documentation for these 32 to show significant changes in their ODI and BMI, and in how many were diagnosed with OSA before and after surgery. Even though it is a small population it still shows significant changes, which would be very interesting to further validate on a bigger population.

We did not find a correlation between the reduction in ODI and the reduction in BMI, which differs from prior studies. Peppard et.al (15) found in their study that a 10% weight gain would predict a 32% increase in AHI, and similarly that a 10% weight loss would predict a 26% decrease in AHI. But this was a study on a normal population with relatively stable weight, and in their study they excluded patients with weight loss or gain over 20%, due to

very small sample size. In their study they also found that the relation between weight and AHI plateaued with greater weight changes. Considering the mean weight of the 32 patients before surgery was 130 [87-173] and 97 [62-132] at the follow up this is a decrease of about 25% which can potentially explain why the decrease in BMI and ODI do not correlate. Another study looking at the impact bariatric surgery has on OSA did also not find any correlation between estimated weight loss (EWL), AHI, and CPAP settings after surgery. (14)

We also did not find a correlation between ODI and BMI before surgery, but it could be hypothesized that this correlation plateaus in a population with obesity, and that the correlation is stronger when comparing a normal weighted population with an obese population. Obesity is a very important risk factor when it comes to developing OSA(9), but there could be a possibility that the degree of obesity is less important.

Conclusion

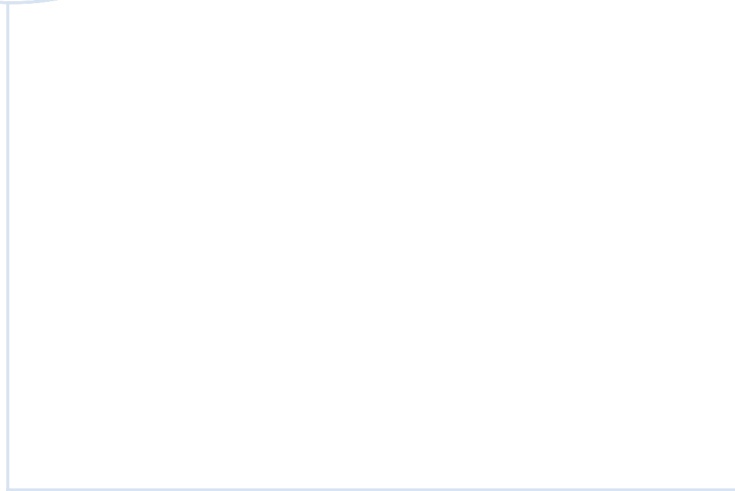
This study shows that patients with sleep apnea prior to bariatric surgery have a strong decrease in severity of OSA and amongst the 32 patients over 80% of them had their OSA resolved, even more than 10 years after they have undergone the surgery. In this study we did not find any correlation between reduction in BMI and reduction in ODI compared to before surgery and at the follow up. Further studies on a bigger population should be performed to validate the long-term effect bariatric surgery has on OSA. It could also be interesting to further investigate how reductions in ODI and BMI correlates with different degrees of weight loss, and how ODI and BMI correlates in populations with obesity, compared to populations without obesity.

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