Predictors of weight loss are different in men and women after sleeve gastrectomy

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Abstract. Introduction - Weight loss following bariatric surgery varies according to patient factors before the intervention. However, whether predictors of weight loss differ between men and women is, to our knowledge, unknown. We therefore aimed to investigate baseline predictors for overall weight loss and identify potential sex-specific baseline predictors in bariatric surgery patients. **Methods** - In this prospective cohort study, 160 patients (117 women and 43 men) who underwent sleeve gastrectomy were followed for two years. Weight loss was defined as percent excess body mass index loss (%EBMIL). To investigate whether %EBMIL differed between men and women, we included all two-way interactions with sex by incorporating the product term sex and predictors using multiple linear regression analysis. **Results** - The overall mean $\pm$ standard deviation of %EBMIL after two years was 78.3 ± 23.5 . Predictors for lower %EBMIL in a regression model with no interactions were female sex ($P = 0.003$), higher body mass index before surgery ($P = 0.001$) and non-smoking ($P = 0.029$). When examining sex-specific predictors for %EBMIL, higher age ($P = 0.027$) and not having diabetes ($P = 0.007$) predicted lower %EBMIL in men. In women, unemployment ($P = 0.006$) and anxiety and/or depression ($P = 0.009$) predicted lower %EBMIL. **Conclusion** - This study suggests that weight loss and predictors for weight loss two years after sleeve gastrectomy are sex-specific. These findings may be useful for the surgical strategy used to treat these patients.

Keywords. Obesity, Predictors, Weight loss, Bariatric surgery, Sleeve gastrectomy

Introduction

Successful weight loss after bariatric surgery is often defined as greater than 50% excess weight loss; however, in the long term, more than 30% of patients fail to achieve this goal [1, 2]. Unsuccessful weight loss is associated with lack of resolution of comorbidities and reduced quality of life [2-4]. Thus, identifying preoperative predictive factors for weight loss might be useful in developing strategies to improve weight loss following bariatric surgery [5]. However, the results from studies evaluating potential predictors of weight loss after bariatric surgery are inconclusive, and further studies with new approaches are needed [1, 5].

We hypothesized that predictors of weight loss after bariatric surgery differ according to sex. If this hypothesis is confirmed, then treatment could be tailored accordingly. However, whether predictors of weight loss after bariatric surgery differ according to sex is, to our knowledge, unknown. What is known and prompted us to perform this study is that men and women differ greatly in terms of fat storage and metabolism [6]. Interestingly, when men and women are asked to explain their inability to lose weight after bariatric surgery, they also seem to emphasize different causes [7]. Thus, there may be “hidden differences” between men and women in terms of weight loss that have been unreported in the literature. Such sex differences could perhaps explain some of the inconsistent results founds in previous studies [1, 5].

Therefore, the aim of this study was to explore potential preoperative predictors (e.g., demographical and clinical variables) of weight loss after sleeve gastrectomy (SG). We hypothesized that predictors for weight loss differed between men and women.

Material and methods

Patients who were accepted for SG at Førde Central Hospital were invited to participate in a prospective cohort study. The criteria for having surgery included BMI ≥ 40.0 or 35.0-39.9 with obesity-related comorbidities, age 18-60, no alcohol or drug problems, no active psychosis and failure to lose weight via other methods. Data were collected at baseline (the preoperative evaluation), preoperatively (the day before surgery), and one and two years after surgery. The study database was approved by the Norwegian Data Inspectorate and conforms to the principles outlined in of the Declaration of Helsinki.

The SG procedure

Prior to SG, patients participated in a one-day course on obesity and bariatric surgery, which was followed by individual consultation with a bariatric surgeon and other health personnel if needed. Preoperative advice included smoking cessation, increased physical activity and weight loss. The operation was performed laparoscopically through six ports, and all vessels at the greater curvature from the pylorus to the cardia were divided by LigaSure (Covidien). The stomach was resected along a 32 French bougie from 2-3 cm proximal to the pylorus to the cardia using a Tri-Stapler (Covidien). Postoperative advice included a low carbohydrate – high protein diet, the intake of one multivitamin tablet daily, a high frequency of water intake and physical activity. Controls and data collection occurred at the outpatient clinic 3, 12 and 24 months postoperatively.

Outcome

The outcome variable percent excess body mass index loss (%EBMIL) (from baseline to two-year follow-up) was calculated using the following formula: $100 - ((\text{follow-up BMI} - 25) / (\text{beginning BMI} - 25)) * 100$ [8]. Body weight was measured in light clothing without shoes to the nearest 0.1 kilogram. Height was measured in a standing position without shoes to the nearest 0.01 meter.

Predictors

Predictors were selected based on previous research [1, 9], theoretical considerations and variable availability. The following predictors were included: Patient age (years), sex, marital status (married/cohabitation versus unmarried/cohabitation), education level (<13 versus ≥ 13 years of education), employment status (unemployed versus employed), time from baseline (preoperative consultation) to surgery (≥ 12 months versus <12 months), BMI at baseline, %EBMIL from baseline to surgery ($\leq 5\%$ versus $>5\%$), smoking (non-smoking versus smoking), diabetes (no versus yes), anxiety and/or depression (no versus yes) and musculoskeletal pain (no versus yes). Due to collinearity, we combined having anxiety and/or depression into one variable. Comorbidities were considered to be present only if the patient's general physician confirmed the diagnosis and the patient was on documented treatment.

Statistics

Statistical analyses were performed using the IBM SPSS version 20 software for Windows. P values were 2-sided, and values <0.05 were considered statistically significant. Continuous variables were described as the mean and standard deviation

(SD), whereas categorical variables were described using the number and percentage. To examine sex-specific changes in BMI over time, we used generalized estimating equations for continuous data. Intra-individual correlation was accounted for using the exchangeable variance-covariance structure. Because of multiple testing, the P values were corrected using the Sidak method.

Simple and multiple linear regression models were constructed using SPSS (using the general linear model-univariate module) to study baseline predictors for %EBMIL after two years. Unstandardized regression coefficients and 95% confidence intervals were reported. To investigate whether predictors of %EBMIL differed between men and women, we included all two-way interactions with sex by incorporating the product term sex and predictor in multivariable models. To obtain sex-specific estimates for predictors that had a significant interaction effect, we ran multiple regression models twice, with men and women coded differently (0 versus 1 and 1 versus 0). The clinical significance (effect size) was estimated for each statistically significant predictor. For continuous variables, we computed the difference in predicted %EBMIL corresponding to a 2-SD difference in predictor variables [10]. For categorical variables, we computed the difference in predicted %EBMIL relative to the reference category. These differences were divided by the SD of the %EBMIL in the entire sample at two years follow-up. These SD units or effect sizes were evaluated against the standard criteria proposed by Cohen: Trivial (<0.2), small (0.2 to <0.5), moderate (0.5 to <0.8), and large (≥ 0.8) [11].

Results

By the two-year follow-up, we had data from 117 women and 43 men (93% follow-up rate) (Table 1 and Figure 1). The BMI significantly changed between all-time points for the entire cohort ($P<0.001$), with the exception of between the one- and two-year follow-ups ($P=0.999$). The mean BMI $\pm$ SD at preoperative evaluation and at the two-year follow-up was 46.8 ± 6.9 and 30.2 ± 5.7 , respectively. The mean $\pm$ SD of %EBMIL at the two-year follow-up was 78.3 ± 23.5 for the entire cohort and 86.9 ± 23.9 and 75.1 ± 22.6 for men and women, respectively (P for sex differences = 0.004).

Multiple regression analysis showed that female sex, higher BMI and non-smoking were significant predictors for lower %EBMIL (Table 2). Interaction analysis showed that the variables age, employment status, diabetes and anxiety and/or depression significantly predicted %EBMIL differently in men and women (Table 3). In men, increasing age and not having a diagnosis of diabetes were significant predictors for lower %EBMIL, while unemployment and a diagnosis of anxiety and/or depression were significant predictors for lower %EBMIL in women (Table

3). The predictive values of the other variables were unaffected by the inclusion of interaction terms (data not shown). The effect sizes for the statistically significant predictors ranged from 0.44 to 0.86 (Table 4). We also performed secondary analysis with %EBMIL at the one-year follow-up as a dependent variable. The directions of the associations were essentially similar but generally much weaker. The only statistically significant findings were that higher BMI at baseline predicted lower %EBMIL and employment status had a different predictive effect on %EBMIL according to sex (data not shown).

Discussion

The principal finding of this study is that age, employment status, diabetes and anxiety and/or depression predicted %EBMIL differently for men and women. When we did not consider sex differences, we found that only female sex, higher preoperative BMI and non-smoking were significant predictors of lower %EBMIL. The gender differences in predictors of weight loss did only manifest themselves two years after surgery.

Using multiple regression analysis not including sex interactions, we observed that women had a lower %EBMIL than men. In general, the literature is inconsistent on this issue [9]. However, as found in this study, a 12.1 percentage point difference in %EBMIL is clinically relevant. We also observed that 18 of the 117 women (16%), but only 1 of the 44 men (2.3%), had a %EBMIL <50%. If these results can be replicated, one hypothesis is that SG may differently influence satiety in men and women.

Our observation that higher BMI at baseline was associated with lower %EBMIL in both sexes is in accordance with a large body of research [1]. This finding is best explained by the fact that high BMI is an indicator of underlying causes of obesity [6]. Thus, a higher BMI indicates that more radical surgery is likely to be needed if a high %EBMIL is to be obtained.

We also observed that non-smoking was associated with lower %EBMIL for both sexes. This association may be related to the effects of smoking on eating behavior and metabolism [12]. However, the limited literature is mixed on whether smoking is associated with greater weight loss after bariatric surgery [9]. Even if there is a small but positive association between smoking and weight loss, the effect of smoking equals having a BMI > 40 in terms of risk for lost life years [13], and this risk of smoking should be communicated to patients.

For the non-significant findings in this study, the lack of association between preoperative weight loss and %EBMIL after two years is perhaps most interesting.

The results in the literature are mixed [1], and we believe that positive associations between preoperative weight loss and weight loss after surgery most likely fade with time [14]. However, we still encourage preoperative weight loss to reduce operative risk.

We will now discuss sex interactions.

First, the observation that men with diabetes had a particularly high %EBMIL is interesting because several studies have shown that having diabetes is associated with lower weight loss after bariatric surgery [9]. Diabetes was not a predictor for %EBMIL in women in this study, but the P-value was borderline significant. A few studies have suggested that men with diabetes may benefit more from behavioral weight reduction programs than women with diabetes, a finding that has been explained by the fact that men with diabetes appear to comply better with treatment regimens [15, 16]. Thus, it is possible that men with diabetes who had bariatric surgery ate less and/or had more physical activity. Nevertheless, our observations suggest that the negative association between diabetes and weight loss after bariatric surgery in the literature may only apply to women.

Second, we observed that increasing age predicted lower %EBMIL in men. Thus, our observations suggest that the negative association between age and weight loss reported in the literature [9] is not independent of sex, and could perhaps be related to declining physical activity as one ages, which may have a particular negative effect on weight loss in men [17]. Thus, men may need to be informed that they are at increased risk for lower weight loss as they age.

Third, we found that unemployment predicted lower %EBMIL in women. The interaction between sex and employment status could be related to differences in work-related behavior. If more men than women travel as a part of their work, working men may thus adhere less to a healthy lifestyle [18]. It is also possible that women who are employed are more physically active than unemployed women. Thus, encouraging and helping patients get back to work may be important for maximizing weight loss if one is able to maintain healthy behaviors.

Finally, we found that women with a diagnosis of anxiety and/or depression had a lower %EBMIL than those without these diagnoses, while no such association was observed for men. Again, the literature of predictors of weight loss is mixed [1], and our observations suggest that not taking sex interactions into account may to some extent explain why. The literature suggests that women with obesity tend to have worse self-reported mental health than men with obesity [19]. If this difference is associated with postoperative eating behavior, it may explain our observations. Unfortunately, we did not have data that allowed us to explore this issue.

The main strengths of this study are the low attrition rate and that the predictor selection for the regression models was based on previous research and included tests for sex interactions. To our knowledge, this is the first study of predictors of %EBMIL after SG that investigates sex interactions for weight loss after bariatric surgery. This study also has limitations that should be addressed. First, we had no data on diet or physical activity after SG. Thus, we do not know whether our set of preoperative predictors was associated with the health behaviors that SG was intended to influence. Furthermore, our set of predictors was not exhaustive, and the male sample size was relatively small, reflecting the fact that fewer men than women choose bariatric surgery. However, the BMI at baseline and standard deviation for %EBMIL after two years were quite similar in men and women. Nevertheless, the results in the male group should be interpreted with caution. Finally, although our study had a longer follow-up than many of the published studies [1], weight regain is more common in the longer term [2]. Therefore, studies with long-term follow-up are clearly needed.

In conclusion, our findings suggest that predictors of weight loss after SG differ for men and women two years after surgery. Further studies should be done to test the external validity of our findings. Thus, we recommend examining sex interactions in future studies on predictors of weight loss after bariatric surgery.

Conflict of interest disclosure statement

No conflict of interest.

Literature

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Tables and figures

Table 1. Patient characteristics

Characteristics	All (N=160)	Women (n=117)	Men (n=43)
Age, years; mean $\pm$ sd.	40.4 $\pm$ 11.1	37.7 $\pm$ 11.1	42.5 $\pm$ 10.9
Married/cohabitation, n (%)	91 (56.9)	71 (60.7)	20 (46.5)
Education ($\geq$ 13 years; n (%))	41 (25.6)	33 (28.2)	8 (18.6)
Employed, n (%)	103 (64.4)	77 (65.8)	26 (60.5)
Waiting time*, $\geq$ 12 months, n (%)	12 (7.5)	11 (9.4)	1 (2.3)
Body mass index, mean $\pm$ sd.	46.8 $\pm$ 6.9	46.8 $\pm$ 6.4	46.6 $\pm$ 8.2
Preop. EBMIL, >5%, n (%)	60 (37.5)	42 (35.9)	18 (41.9)
Smoking, n (%)	31 (19.4)	23 (19.7)	8 (18.6)
Musculoskeletal pain, n (%)	72 (45.0)	51 (43.6)	21 (48.8)
Diabetes, n (%)	32 (20.0)	20 (17.1)	12 (27.9)
Mental disorder, n (%)	36 (22.5)	26 (22.2)	10 (23.3)

Note: EBMIL: excess body mass index loss. *: Waiting time is defined as the time from preoperative evaluation to surgery.

Table 2. Linear regression analysis with percent excess body mass index loss after two years as the dependent variable (N=160)

Dependent variables	Simple regression		Multiple regression	
	B (95% CI)	P-value	B (95% CI)	P-value
Age (years)	-0.2 (-0.5, 0.1)	0.260	-0.2 (-0.5, 0.2)	0.318
Sex (ref. men)	-11.8 (-19.9, -3.7)	0.004	-12.1 (-20.0, -4.2)	0.003
Married/cohabitation (ref. no)	0.8 (-6.7, 8.2)	0.841	-0.3 (-7.4, 6.8)	0.926
Education (ref. <13 years)	-3.3 (-11.7, 5.1)	0.436	-3.4 (-11.6, 4.7)	0.411
Employed (ref. no)	-7.1 (-14.7, 0.5)	0.065	-5.0 (-12.8, 2.8)	0.204
Waiting time * (ref. >12 months)	-6.8 (-20.7, 7.1)	0.336	-3.1 (-16.3, 10.2)	0.648
BMI (units at baseline)	-1.1 (-1.6, -0.6)	<0.001	-0.9 (-1.4, -0.4)	0.001
%EBMIL (ref. ≤ 5%)	-0.3 (-7.9, 7.3)	0.945	3.3 (-4.2, 10.9)	0.385
Smoking (ref. no)	13.3 (4.3, 22.4)	0.004	10.3 (1.1, 19.5)	0.029
Diabetes (ref. no)	1.4 (7.8, 10.6)	0.764	0.9 (-8.0, 9.7)	0.848
Mental disorder (ref. no)	-8.0 (-16.7, 0.8)	0.073	-7.0 (-15.5, 1.5)	0.105
Musculoskeletal pain (ref. no)	-0.0 (-7.4, 7.3)	0.991	-0.7 (-7.7, 6.4)	0.854

Note: Waiting time is defined as the time from preoperative evaluation to surgery. Adjusted $R^2 = 15.6\%$.

Table 3. Gender-specific linear multiple regression analysis with percent excess body mass index loss after two years as the dependent variable (N=160)

Predictors	B (95% CI)	P-value
Gender x age interaction	NA	0.047
Age (years)		
Men	-0.8 (-1.3, -0.8)	0.027
Women	0.2 (-0.4, 0.4)	0.925
Gender x employment interaction	NA	0.001
Employed (ref. no)		
Men	-13.1 (-26.3, 0.3)	0.054
Women	12.4 (3.6, 21.1)	0.006
Gender x diabetes interaction	NA	0.002
Diabetes (ref. no)		
Men	20.2 (5.5, 34.9)	0.007
Women	-9.1 (-19.7, 1.5)	0.092
Gender x Anxiety and/or depression interaction	NA	0.017
Anxiety and/or depression (ref. no)		
Men	9.2 (-6.5, 24.9)	0.250
Women	-13.0 (-22.7, -3.3)	0.009

Note: Only sex-specific estimates from significant gender interactions are presented. The estimates are adjusted for the baseline values for age, gender, marital status, education, waiting time, body mass, preoperative percent excess weight loss, smoking, diabetes, anxiety and /or depression and musculoskeletal pain. NA: not applicable.

Table 4. Effect sizes of statistically significant predictors of %EBMIL

Predictors	Effect size
General predictors	
Sex (ref. men)	-0.51
Body mass index (per 2 SD)	-0.58
Smoking (ref. no)	0.44
Predictors only in men	
Higher age (per 2 SD)	-0.72
Diabetes (ref. no)	0.86
Predictors only in women	
Employed (ref.no)	0.53
Having anxiety and/or depression (ref.no)	-0.55

Note: For the continuous variables, we computed the difference in predicted percent excess body mass index loss (%EBMIL) corresponding to a 2-SD difference in the predictor variables. For categorical variables, we computed the difference in predicted %EBMIL relative to the reference category. These differences were divided by 23.5 (the SD of the %EBMIL in the entire sample at two years follow-up). Effect sizes were judged against the standard criteria proposed by Cohen: trivial (<0.2), small (0.2 to <0.5), moderate (0.5 to <0.8), and large (≥ 0.8)

Figure 1. Means and standard deviations for body mass index in men (n=43) and women (n=117). Pre.op: preoperative. 1 y: 1 year. 2 y: 2 years.