OUTCOMES FOLLOWING LAPAROSCOPIC ROUX-EN-Y GASTRIC BYPASS (LRYGB) VARY BY SEX: ANALYSIS OF 83,059 MORBIDLY OBESE WOMEN AND MEN

Malinda Lyon, Chris Bashian, Casey Sheck, Leon Kushnir and Gus J Slotman

Department of Surgery, Inspira Health Network

1505 West Sherman Avenue, Vineland, NJ

Corresponding author:

Gus J Slotman, M.D., FACS, FCCM, FCCP, FASMBS

Director of Clinical Research

Inspira Health Network

Clinical Professor of Surgery Rowan University

1505 West Sherman Avenue, Suite B

Vineland, New Jersey 08028

Tel: 856-641-8635

Fax: 856-641-8636

Email: slotmang@ihn.org

Presented at the 2018 Southwestern Surgical Congress

April 8-11, 2018, Napa, California

Summary: Clinical outcomes following LRYGB vary significantly between men and women. In spite of greater weight loss, at 12 months BMI was higher for men. Women persisted higher in 5 main categories. Men resolved cardiopulmonary/vascular issues and metabolic derangements less, and developed abdominal hernia, and were functionally impaired more than women. Higher alcohol consumption may contribute to increased male liver disease. Overall, women may benefit more from LRYG than do men.

ABSTRACT

Background: Previously we have reported variation in pre-operative clinical characteristics between women and men undergoing laparoscopic roux-en-Y gastric bypass (LRYGB). However, variation by sex in post-operative outcomes following LRYGB has not been investigated.

Methods: Pre-operative data was compared to follow-up data at 12 months after surgery on 83,059 patients from the Surgical Review Corporation's BOLD database. Data included age, weight, BMI, and 31 obesity-related medical conditions.

Results: Men had increased weight, actual weight lost, and BMI. Women had higher rates of gastrointestinal and mental health disorders. Men failed to resolve cardiopulmonary/vascular and metabolic derangements, abdominal hernia, and were more functionally impaired than women.

Conclusions: Overall, women may benefit more from LRYG than men, as their pre-operative conditions showed greater improvement at 12 months post-op. This advance knowledge may aid LRYGB planning and improve outcomes.

Keywords: Obesity; Roux-en-Y; Gender; Co-morbidities; Bariatric surgery

INTRODUCTION

The obesity epidemic has brought bariatric surgery into the daily conversations of physicians across specialties. The numbers coming from the World Health Organization are staggering, with world-wide obesity tripling since 1975 and adult obesity at 13% in 2016 (BMI $\geq$30 kg/M^2)[1]. A multitude of obesity associated comorbidities have been identified[2,3], leading to 4.0 million deaths globally in 2015, 7.1% of deaths from any cause[4]. The concerns for these patients involve not only the obesity related comorbidities but also patient quality of life (QoL). It is because of these findings that bariatric surgery has been a hot topic for surgical research. In previous studies only bariatric surgery improves weight loss, obesity related co-morbidities,[5,6] as well as QoL[7,8]. Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) has been the gold standard for surgical treatment of obesity. LRYGB has comparable reduction in obesity related co-morbidities and superior improvement in physical function[9] as well as increased remission of gastroesophageal reflux symptoms[10] compared to sleeve gastrectomy (SG).

As more results and studies have been published the positive outcomes in co-morbidity reduction and weight loss are no longer questioned, however as demonstrated in further investigation, variations in the pre-operative patient profile between men and women exist. Recent studies validate that prior to LRYGB women have increased rates of cholelithiasis, mental health diagnosis and somatic pain complaints. This is in contrast to men having significantly higher cardio-pulmonary and metabolic comorbidities as well as liver disease. The pre-operative LRYGB male patient is also older with higher rates of tobacco and alcohol use[11].

Outcomes from LRYGB have been published in mass, however outcomes based purely on sex are rare. It has been substantiated that after LRYGB men are 2.5 times more likely to decrease the number of medications being taken[12]. Kennedy et al. also documented women as more likely to continue taking mental health medication, specifically antiepileptic medications[12]. It is because of the paucity of data comparing male vs female outcomes in these complex and medically fragile patients that this study was undertaken. The objective of this study was to identify significantly statistical and clinical variations in the long-term outcomes between women and men who underwent LRYGB.

MATERIALS AND METHODS

Pre-operative and follow-up data at 2, 6, 12, 18 and 24 months after surgery on 83,059 patients from the Surgical Review Corporation's BOLD database who underwent LRYGB was analyzed retrospectively in two groups: Women (n=65,325) and Men (n=17,734).

Data included age, weight, BMI, and 31 weight-related medical conditions including hypertension (HTN), angina, congestive heart failure (CHF), peripheral vascular disease (PVD), obstructive sleep apnea (OSA), obesity hypoventilation syndrome (OHS), asthma, ischemic heart disease, abdominal hernia, abdominal panniculitis, cholelithiasis, gastroesophageal reflux disease (GERD), liver disease, stress urinary incontinence, diabetes mellitus, gout, dyslipidemia, pseudotumor cerebri, back pain, lower extremity edema and musculoskeletal pain, mental health diagnoses,

impaired functional status, depression, psychological impairment, alcohol use, substance abuse, tobacco use, and fibromyalgia.

Statistical analysis: Continuous variables were analyzed using ANOVA with baseline and treatment in the model. Pair-wise comparisons were performed on the least squares means of the treatments calculated from the ANOVA model to find differences in the treatment groups. Distribution of obesity co-morbidities was examined by a general linear model with baseline and treatment in the model, and modified for binomial distribution to account for dichotomous variables. (SAS/STAT(R) 9.22 User's Guide, 2009. The SAS Institute, Cary, NC)

RESULTS

Pre-operatively 83,059 morbidly obese patients were divided into two groups based on sex, with 65,325 women and 17,734 men. At 2, 6, 12, 18, and 24 months post operatively 63,625, 36,708, 20,755, 5,472, and 4,316 women were available for analysis, respectively, as were 17,333, 9,816, 5,390, 1,356, and 1,049 men.

Weight, BMI, and weight loss are displayed in Table 1. Males weighed more both pre- and post-operatively as well as had higher BMI. Total weight loss was higher for males vs. females at 2, 4, 6,12,18, and 24 months, but, nevertheless, weight and BMI remained higher also.

Cardiopulmonary obesity co-morbidities are tabulated in Table 2. Among males OHS and PHT were more frequent than in women at 12 months, while CHF, PVD, HTN,

OSA, and angina remained elevated in men through 24 months. Women had a higher incidence of asthma.

Metabolic and endocrine co-morbidities are listed in Table 3. Although by 24 months after LRYGB diabetes mellitus had resolved among men threefold from 49.9% to 15.25%, diabetes remained higher among males versus female, as did gout, and dyslipidemia. Females maintained higher incidence of pseudotumor cerebri.

Abdominal and hepatobiliary co-morbidities are seen in Table 4. Cholelithiasis, abdominal panniculitis, gastroesophageal reflux disease (GERD), and stress urinary incontinence were higher in women through 24 months. Liver disease and abdominal hernia were increased for men compared with women through 12 months.

Somatic co-morbidities are presented in Table 5. Baseline variation by sex in back pain and musculoskeletal pain resolved by 6 months. Lower extremity edema did not vary by sex.

Psychological and Behavioral co-morbidities are summarized in Table 6. Mental health diagnosis, depression, and psychological impairment were higher in women through 24 months, as, conversely, was support group attendance. Substance abuse, smoking and alcohol consumption were higher for men.

DISCUSSION

The results of this study identify statistically and clinically significant variations in clinical characteristics and post-operative outcomes between men and women who underwent LRYGB. In spite of greater weight loss, male weight and BMI remained higher than women through 24 months. Cardiovascular issues resolved less with weight

loss among men than women, with increased male congestive heart failure, hypertension, angina, peripheral vascular disease, and dyslipidemia persisting through 24 months and pulmonary hypertension to 12 months. Pulmonary conditions of obesity hypoventilation syndrome and obstructive sleep apnea affected men more often, with sleep apnea increased versus women at 24 months. Asthma was higher for women throughout the study. Elevated male alcohol consumption to 24 months may have contributed to increased liver disease to 12 months. Substance and tobacco abuse were higher in men. Abdominal hernia developed more frequently in men, while cholelithiasis, GERD, stress urinary incontinence, and abdominal panniculitis were increased among women. The endocrine and metabolic co-morbidities diabetes mellitus and gout resolved significantly less throughout for men versus women. At up to 12 months, impaired function and lower extremity edema were increased in males. Women experienced persistently increased mental health issues, depression, and psychological impairment compared with men. Twelve months after LRYGB men had higher prevalence of 17 weight-related problems versus women, while women retained nine co-morbidities at increased levels. Men resolved ten problems less than women at 24 months, with women persisting in 8. Our review of the literature indicates that these variations by sex in resolution of the major obesity co-morbidities following LRYGB have not been reported previously, and are important findings of this investigation.

Women far exceeded men in number for those who underwent LRYGB in this study, consistent with a trend noted previously in bariatric surgery overall[13]. This phenomenon has been attributed to differences socioeconomically, demographically[14], as well as physician recommendation[15]. Health improvements were noted in a

predominantly male population undergoing gastric bypass in a study performed by Gisella Carranza-Leon B, et al.[16] and men were found to be as willing to consider bariatric surgery when recommended by their doctor[15]. Interestingly the present study found that, in spite of greater weight loss, male weight and BMI remained higher than women through 24 months. While the higher overall weight in men might have been expected, that BMI for men did not fall commensurate with that of women after LRYGB suggests that in these parameters, men benefitted somewhat less than women from the procedure.

Furthermore, again in spite of greater weight loss than women in this study, men undergoing LRYGB failed to resolve cardiovascular issues in the same proportion. Compared with females, male congestive heart failure, hypertension, angina, peripheral vascular disease, and dyslipidemia persisting through 24 months, and pulmonary hypertension to 12 months. Whether or not higher male tobacco abuse was a factor is not clear from the data. Nevertheless, this constellation of factors should be considered in the bariatric surgical management of morbidly obese men.

Morbidly obese men undergoing LRYGB also resolved serious pulmonary co-morbidities less well than women. Our data revealed that LRYGB reduced OHS and, more importantly, OSA dramatically overall, but also that the OSA incidence at 24 months remained significantly higher among men which may be related to increased tobacco use[17], non-resolution of diabetes mellitus[18], or to anatomical differences in the upper airway of men vs women[19]. Conversely, from baseline through 24 months, female asthma was significantly greater than for men. It has been suggested that asthma in the obese is of different pathophysiology than other types of asthma[20] and that women are

more susceptible than men to develop asthma in relation to weight gain[21] which may be influenced by sex hormones as well as increased visceral adipose tissue leading to increased cytokines in women[22,23]. Our results are consistent with this theory.

Non-alcoholic fatty liver disease is a common complication of severe obesity, and can be improved with weight loss following bariatric surgery[24], possibly also contributing to decreased development of liver cancer among bariatric surgery patients compared with non-operated morbidly obese[25]. In the present study, liver disease affected more men than women through 12 months follow-up after LRYGB. To our knowledge, this variation by sex in the prevalence of post-LRYGB liver disease has not been reported previously. While evidence suggests that a significant minority of individuals who undergo Roux-en-Y gastric bypass experience problematic alcohol and substance use following surgery[26], prior studies have not observed increased alcohol consumption in male LRYGB patients identified in this investigation. One might speculate that increased male versus female alcohol consumption through 24 months in this study could have contributed to the elevated rates of post-operative liver disease in men.

In addition to liver disease, other abdominal and hepatobiliary co-morbidities varied by sex in this investigation. Abdominal hernias appeared more often in men early after LRYGB but as weight loss continued for both sexes, this variation resolved by 24 months. Women, in contrast, experienced higher GERD, which difference resolved by 24 months, and increased cholelithiasis, abdominal panniculitis, and stress urinary incontinence throughout the study. The greater prevalence of cholelithiasis long-term after LRYGB among women in this study suggests that the increased propensity of women overall to develop gallstones[27] is not alleviated by post-bariatric surgery weight

loss. Similarly, constantly increased stress urinary incontinence in women over men observed here is consistent with prior work indicating that although bariatric surgery reduced urinary incontinence[28], the persistence of stress urinary incontinence post operatively remained a co-morbidity for females more so than for males[29]. Increased panniculitis among women in this study, whose weight and BMI were smaller than men, contrast with reports of a direct relationship between body mass and pannus-related complication rates[30]. The mechanism for this finding is not clear from the data.

Following LRYGB, diabetes resolved threefold in both women and men, but at 24 months it was still significantly higher in males versus females. While this variation may be related in part to pre-operative diabetes incidence, that diabetes persisted long-term more prominently in men than women suggests that males may benefit less than females in curing diabetes after LRYGB. Whether or not further lowering male BMI following LRYGB with more vigorous post-operative attention to bariatric diet and exercise would bridge this gender gap is not clear from the literature or the data. Pre-operatively LRYGB men were older than women[11], which could be a contributing factor. Improvement in diabetes regardless of weight loss after RYGB was noted in the study performed by Li QR, et al.[31] which was seen in our results of greater weight loss but less resolution of diabetes mellitus in men compared to women. Dyslipidemia affected men most throughout the study, as did gout which continues to be a more prominent condition in non-obese, obese, and post RYGB bariatric men[11,32]. Variation by sex of these serious problems suggests that men may fare less well than women in endocrine and metabolic co-morbidities.

Short-term increased somatic co-morbidities in men, including impaired function

and lower extremity edema, are consistent with the concept that men are affected more adversely by obesity than are women. It suggests also that the benefits of LRYGB might be fewer for men.

The higher incidence of mental health issues, depression, psychological impairment with the decreased weight loss but lower BMI seen in women vs men postoperatively from LRYGB may be explained partially by the findings of Miller-Matero LR et al. who found emotional eating and food addiction seen pre-operatively correlated to less weight loss at the 1 year post-operative mark[33]. While depression was still a more prominent issue for females more than men following LRYGB, nevertheless our study and the one performed by Elias K, et al. did both observe overall a decrease in depression after gastric bypass[34].

Twelve months after LRYGB men had a higher prevalence of seventeen weight-related problems versus women, while women retained nine co-morbidities at increased levels over men. Men resolved ten problems less than women at 24 months, with women persisting in eight. Based on the outcomes from our data, the prevalence of co-morbidities increased in men over women post-operatively, and the specific co-morbidities that women resolve less effectively than men should be considered when post-operative expectations are discussed with patients considering LRYGB.

There were several limitations to our study. This is a retrospective analysis of prospectively collected data, and, as such, carries many typical confounders. In addition, the patients in this study represent a self-selected population, and therefore, the findings might not extrapolate directly to other bariatric operations. Diagnosis of co-morbidities in BOLD was based on a clinical diagnosis or was self-reported by patients,

rather than derived from a pathological diagnosis, such as liver biopsy, for example. The follow-up study population did decrease at each time period recorded post-operatively. Nevertheless, there were over 5,300 patients in our final follow up period 24 months post-op.

CONCLUSIONS

Clinical outcomes following LRYGB vary significantly between men and women. In spite of greater weight loss, BMI was higher for men. Women persisted in higher cholelithiasis, abdominal panniculitis, GERD, and stress incontinence, and in serious mental health conditions. Men failed to resolve clinically important cardiopulmonary/vascular issues, metabolic derangements (diabetes, gout, dyslipidemia), developed abdominal hernia, and were functionally impaired more than women. Increased alcohol consumption may have contributed to increased male liver disease. Overall, women may benefit more from LRYGB than do men. The advance knowledge from these results may facilitate optimized pre-operative counseling and planning as well as post-LRYGB management.

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Table 1: Weight, Weight Loss and BMI after Laparoscopic Roux-en-Y Gastric Bypass by Sex						
WEIGHT (kg) (SD)	Baseline	2 months	6 months	12 months	18 months	24 months
Female	**126.9** **22.72**	**110.9** **21.3**	**92.65** **18.69**	**82.07** **17.24**	**79.79** **17.29**	**79.9** **17.25**
Male	**155.9** **29.51**	**134.1** **27.21**	**113.1** **23.35**	**103.6** **20.69**	**101.4** **20.14**	**101.5** **19.69**
p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
WEIGHT LOSS (kg) (SD)	Baseline	2 months	6 months	12 months	18 months	24 months
Female	**n/a** **n/a**	**15.99** **7.318**	**34.23** **9.314**	**44.86** **13.13**	**47.43** **15.46**	**46.33** **15.61**
Make	**n/a** **n/a**	**21.75** **10.11**	**42.93** **13.29**	**53.24** **18.94**	**53.91** **21.17**	**53.92** **21.68**
p-value	**n/a**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
BMI (SD)	Baseline	2 months	6 months	12 months	18 months	24 months
Female	**47.28** **7.72**	**41.31** **7.32**	**34.5** **6.492**	**30.62** **6.081**	**29.84** **6.153**	**29.87** **6.064**
Male	**48.96** **8.61**	**42.11** **8.013**	**35.53** **6.857**	**32.48** **6.058**	**31.88** **5.941**	**32.08** **5.877**
p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
SD= Standard Deviation; BMI= Body Mass Index						

Table 2: Cardio-Pulmonary Comorbidities after Laparoscopic Roux-en-Y Gastric Bypass by Sex

Months	Sex	CHF	PVD	PHT	Asthma	HTN	OSA	ANGINA	OHS
Baseline	Female	1.78%	0.97%	4.79%	20.34%	56.93%	43.32%	2.59%	1.68%
	Male	4.12%	2.01%	5.46%	12.77%	73.22%	65.35%	3.95%	2.63%
	p-value	<0.0001	<0.0001	0.0002	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
2	Female	1.76%	0.90%	3.48%	18.26%	46.80%	37.25%	2.00%	1.40%
	Male	3.92%	1.79%	3.94%	11.48%	61.03%	57.54%	3.25%	2.26%
	p-value	<0.0001	<0.0001	0.0041	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
6	Female	1.65%	0.79%	1.94%	16.45%	37.22%	28.81%	1.61%	1.20%
	Male	3.56%	1.60%	2.41%	10.74%	49.05%	45.17%	3.00%	1.98%
	p-value	<0.0001	<0.0001	0.0034	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
12	Female	13.70%	0.81%	1.32%	14.92%	31.20%	22.69%	1.40%	1.17%
	Male	3.23%	1.48%	1.67%	10.02%	41.50%	34.97%	3.03%	1.89%
	p-value	<0.0001	<0.0001	0.0478	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
18	Female	1.37%	0.75%	1.26%	15.25%	28.04%	19.93%	1.30%	1.26%
	Male	2.95%	1.47%	1.18%	8.92%	39.38%	32.37%	3.32%	1.70%
	p-value	<0.0001	0.0111	0.8086	<0.0001	<0.0001	<0.0001	<0.0001	0.2139
24	Female	1.34%	0.79%	1.11%	14.24%	26.76%	18.39%	1.30%	1.32%
	Male	3.24%	1.62%	1.62%	8.96%	36.42%	26.02%	2.76%	1.62%
	p-value	<0.0001	0.0127	0.1778	<0.0001	<0.0001	<0.0001	0.0007	0.4566

CHF= Congestive Heart Failure; PVD= Peripheral Vascular Disease; PHT= Pulmonary Hypertension; OSA= Obstructive Sleep Apnea; OHS= Obesity Hypoventilation Syndrome;

Table 3: Metabolic and Endocrine Comorbidities after Laparoscopic Roux-en-Y Gastric Bypass by Sex					
Months	**Sex**	DM	Gout	Dyslipidemia	Pseudotumor Cerebri
Baseline	**Female**	**35.94%**	**2.49%**	**40.88%**	**2.72%**
	Male	**49.94%**	**8.38%**	**52.62%**	**0.92%**
	p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
2	**Female**	**25.19%**	**2.08%**	**35.83%**	**2.22%**
	Male	**35.79%**	**7.58%**	**46.45%**	**0.76%**
	p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
6	**Female**	**17.70%**	**1.68%**	**29.99%**	**1.73%**
	Male	**25.89%**	**6.98%**	**38.74%**	**0.55%**
	p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
12	**Female**	**13.21%**	**1.55%**	**25.17%**	**1.88%**
	Male	**19.90%**	**6.89%**	**32.52%**	**0.59%**
	p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
18	**Female**	**11.44%**	**1.39%**	**23.24%**	**2.08%**
	Male	**17.70%**	**6.27%**	**30.90%**	**0.22%**
	p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
24	**Female**	**10.41%**	**1.37%**	**21.91%**	**2.20%**
	Male	**15.25%**	**4.77%**	**29.27%**	**0.38%**
	p-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**

DM= Diabetes Mellitus;

Table 4: Abdominal and Hepatobiliary Comorbidities after Laparoscopic Roux-en-Y Gastric Bypass by Sex

Months	Sex	Cholelithiasis	Abdominal Panniculitis	GERD	Liver Disease	Stress Urinary Incontinence	Abdominal Hernia
Baseline	Female	24.86%	7.99%	51.54%	6.88%	30.18%	4.41%
	Male	9.47%	6.43%	43.11%	8.29%	4.24%	7.58%
	p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
2	Female	24.51%	7.63%	39.09%	6.72%	24.00%	4.31%
	Male	9.57%	6.16%	33.00%	7.95%	3.39%	7.24%
	p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
6	Female	24.91%	8.10%	29.18%	6.37%	19.83%	4.29%
	Male	10.20%	6.49%	24.63%	7.90%	2.92%	7.31%
	p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
12	Female	25.87%	8.79%	25.12%	6.16%	17.50%	4.53%
	Male	10.34%	6.98%	20.97%	7.57%	2.56%	7.35%
	p-value	<0.0001	<0.0001	<0.0001	0.0002	<0.0001	<0.0001
18	Female	26.20%	10.16%	24.42%	6.71%	16.76%	4.29%
	Male	11.06%	8.26%	20.21%	7.08%	2.51%	6.42%
	p-value	*<0.0001*	0.0346	0.0011	0.6273	<0.0001	0.0017
24	Female	25.57%	7.81%	22.40%	4.52%	15.93%	5.12%
	Male	10.01%	4.86%	20.11%	4.29%	2.86%	6.39%
	p-value	*<0.0001*	0.0009	0.1091	0.7451	<0.0001	0.1037

GERD= Gastroesophageal Reflux Disease

Table 5: Somatic Comorbidities after Laparoscopic Roux-en-Y Gastric Bypass by Sex

Months	Sex	Back Pain	Lower Extremity Edema	Musculoskelatal Pain
Baseline	Female	50.46%	30.14%	46.81%
	Male	47.74%	30.38%	44.99%
	p-value	<0.0001	0.5359	<0.0001
2	Female	43.71%	22.09%	39.23%
	Male	41.57%	22.97%	38.23%
	p-value	<0.0001	0.0136	0.0163
6	Female	36.52%	17.18%	33.39%
	Male	35.45%	18.28%	32.39%
	p-value	0.0503	0.0106	0.0608
12	Female	32.67%	14.79%	29.78%
	Male	32.29%	16.30%	28.95%
	p-value	0.5986	0.006	0.2343
18	Female	29.43%	14.22%	27.00%
	Male	29.50%	14.82%	26.70%
	p-value	*0.9624*	0.5726	0.8203
24	Female	29.70%	13.01%	26.25%
	Male	28.98%	13.35%	25.64%
	p-value	*0.6463*	0.7703	0.6902

Table 6: Psychological and Behavioral Comorbidities after Laparoscopic Roux-en-Y Gastric Bypass by Sex

Months	Sex	Mental Health Diagnosis	Support Group Attendance	Depression	Tobacco Use	Psychological Impairment	Substance Abuse	Alcohol Use
Baseline	Female	12.45%		39.80%	6.18%	19.06%	0.39%	29.94%
	Male	7.32%		25.05%	0.00%	12.99%	0.67%	34.72%
	p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
2	Female	11.90%	17.12%	37.22%	4.87%	18.12%	0.33%	21.64%
	Male	7.06%	16.03%	23.14%	6.62%	12.21%	0.55%	25.49%
	p-value	<0.0001	0.0007	<0.0001	<0.0001	<0.001	<0.0001	*<0.0001*
6	Female	10.84%	17.39%	35.07%	4.52%	16.56%	0.32%	20.54%
	Male	6.49%	16.17%	21.33%	6.43%	11.08%	0.65%	25.16%
	p-value	<0.0001	0.0042	<0.0001	<0.0001	<0.001	<0.0001	*<0.0001*
12	Female	10.50%	16.84%	34.06%	4.35%	15.94%	0.31%	20.56%
	Male	6.63%	15.90%	21.03%	5.20%	11.01%	0.59%	25.30%
	p-value	<0.0001	0.099	<0.0001	0.008	<0.001	0.0026	*<0.0001*
18	Female	10.64%	14.89%	33.55%	4.00%	16.20%	0.24%	19.27%
	Male	6.56%	14.01%	19.54%	4.28%	10.91%	0.81%	24.04%
	p-value	*<0.0001*	*0.4117*	<0.0001	0.6476	<0.001	0.0014	<0.0001
24	Female	11.38%	14.13%	35.40%	5.70%	16.58%	0.30%	20.03%
	Male	6.10%	11.53%	20.02%	5.91%	10.68%	0.38%	27.65%
	p-value	*<0.0001*	*0.0278*	<0.0001	0.0689	<0.001	0.6797	<0.001