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Short-term Changes in Insulin Resistance following Weight Loss Surgery for Morbid Obesity: Laparoscopic Adjustable Gastric Banding versus Laparoscopic Roux-en-Y Gastric Bypass

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Background: Laparoscopic adjustable gastric banding (LAGB) and laparoscopic Roux-en-Y gastric bypass (LRYGBP) both effectively treat the insulin resistance associated with type 2 diabetes mellitus (T2DM). Restriction of caloric consumption, alterations in the entero-insular axis or weight loss may contribute to lowering insulin resistance after these procedures. The relative importance of these mechanisms, however, following LAGB and LRYGBP remain unclear. The aim of this study was to compare directly the short-term changes in insulin resistance following LAGB and LRYGBP in similar populations of patients.

Methods: Patient preference determined operation type. The Homeostasis Model Assessment for Insulin Resistance (HOMA IR) was used to measure insulin resistance. Preoperative values were compared to postoperative levels obtained within 90 days of surgery. Significant differences between groups were tested by ANOVA.

Results: There were no significant preoperative differences between groups. The 56 LAGB patients had a mean age of 42.5 years (25.7-63), BMI of 45.5 kg/m^2 (35-66) and preoperative HOMA IR of 4.1 (1.4-39.2). 75% of LAGB patients were female and 43% had T2DM. The 61 LRYGBP patients had a median age of 39.9 years (22.1-64.3), BMI of 45.0 kg/m^2 (36-62), and preoperative HOMA IR of 5.0 (0.6-56.5). 79% of LRYGBP patients were women and 44.3% had T2DM. Median follow-up for LAGB patients was 45 days (18-90) and for LRYGBP patients 46 days (8-88 days). LAGB patients had a median of 14.8 % excess weight loss (6.9%-37.0%) and LRYGB patients 24.2% (9.8%-51.4%). Postoperative HOMA IR was significantly less after LRYGBP, 2.2 (0.7-12.2), than LAGB, 2.6 (0.8-29.6), although change in HOMA IR was not significantly different. Change in HOMA IR for both groups did not vary with length of follow-up or weight loss but correlated best with preoperative HOMA IR (LAGB r=0.8264; LRYGBP r=0.9711).

Conclusions: Both LAGB and LRYGBP significantly improved insulin resistance during the first 3 months following surgery. Both operations generated similar changes in HOMA IR, although postoperative HOMA IR levels were significantly lower after LRYGBP. These findings suggest that caloric restriction plays a significant role in improving insulin resistance after both LAGB and LRYGBP.

Key words: Bariatric surgery, morbid obesity, laparoscopic adjustable gastric banding, laparoscopic gastric bypass, weight loss, diabetes mellitus, insulin resistance, HOMA IR

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Introduction

Weight loss surgery causes clinical resolution of type 2 diabetes mellitus (T2DM) in most patients.[1] In 1983, Sanderson and colleagues[2] first documented the impact of jejuno-ileal bypass on T2DM.[2] In 1991, Deitel's group[3] and Mason's group[4] both reported rapid clinical improvement of T2DM following vertical banded gastroplasty at the 8th Annual Meeting of the American Society of Bariatric Surgery. In 1992, Pories presented his success with treating T2DM with gastric bypass.[5] In 1998, Scopinaro and colleagues[6] demonstrated the reversal of insulin resistance by biliopancreatic diversion. More recently, in 2002, Dixon and

O'Brien[7] established that laparoscopic adjustable gastric banding (LAGB) also effectively treated T2DM. Although all varieties of bariatric operations appear to treat T2DM, disagreement exists regarding the relative effectiveness and mechanisms of actions of these different operations.

Several mechanisms may mediate the effect of bariatric surgery on T2DM.[1,8,9] Calorie-restricted diets, changes in the entero-insular axis and weight loss all favorably impact clinical T2DM and insulin resistance. In 1996, Deitel first pointed to the role of early postoperative very low calorie diets in the improvement of insulin resistance following vertical banded gastroplasty.[10] In contrast, Sirinek and colleagues[11] had argued in 1986 that changes in levels of gut peptides participating in the entero-insular axis modulated the decreased insulin resistance observed following gastric bypass. Rubino and colleagues have recently supported this hypothesis with careful studies in both gastric bypass patients[12] and an animal model of T2DM.[13] Scopinaro's group has pointed to the importance of long-term weight loss, and specifically fat loss, in the long-term reversal of insulin resistance by biliopancreatic diversion.[14] Nonetheless, the relative importance of each of these mechanisms for each specific bariatric operation remains ill-defined.

The purpose of this paper is to compare short-term changes in insulin resistance following two different bariatric operations that cause weight loss by different mechanisms. LAGB restricts calorie intake while laparoscopic Roux-en-Y gastric bypass (LRYGBP) both restricts caloric intake and bypasses much of the foregut, thereby possibly favorably impacting the entero-insular axis. We hypothesized that if LRYGBP causes improvement in insulin resistance by both caloric intake restriction and changes in the entero-insular axis, then short-term changes in insulin resistance following LRYGBP should be significantly greater than changes following LAGB. In this study, we found that changes in insulin resistance for the first 3 months following LRYGBP and LAGB were similar. These findings suggest that caloric restriction alone may significantly contribute to changes in a resistance following both LAGB and LRYGBP.

Methods

Patient Selection: Between August 2004 and October 2005, one surgeon (GHB) performed 161 weight loss operations for morbid obesity. Of these 161 operations, 76 patients (48%) underwent LAGB and 85 (52%) LRYGBP. All patients met the criteria detailed by the National Institutes of Health for patient selection to undergo weight loss surgery for morbid obesity. Patient preference determined type of surgery performed. All operations were accomplished laparoscopically. There were no deaths. Only patients with complete data sets for preoperative and postoperative fasting serum glucose and insulin were included in the study. Postoperative values were required for only the first 90 days following surgery. Only the first postoperative values were included if more than one set had been obtained. A total of 117 patients (73%) met these criteria: 56 of the 76 (74%) LAGB patients and 61 of the 85 (72%) LRYGBP patients. The most common reasons for incomplete data sets were patient failure to undergo blood testing and failure of the clinical laboratories to perform the requested tests.

Data Collection: Preoperative blood levels were obtained within 30 days of surgery. Preoperative weights were obtained 1-3 days before surgery in the surgeon's (GHB) office. Patients were asked to return for follow-up visits at 1 week, 3 weeks, 6 weeks and 3 months following surgery. Patients were weighed at each visit. Follow-up blood tests were requested usually at the 3-week and 3-month visits. All data were prospectively entered into a data-base as part of the routine care of bariatric surgery patients as approved by our Institutional Review Board.

Data Analysis: All data is presented as medians and minimum and maximum values. Kruskal-Wallis one-way analysis of variance (ANOVA) identified significant differences between groups. Dunn's multiple comparison tests identified significant differences between groups when more than two groups were compared. Chi-square tested for significant differences between distribution of race, ethnicity and co-morbid diseases. Heterogeneity of regression tested the significance between differences in slope and intercept for first degree linear regressions. All tests were performed with a commercially available computer statistics package (Unistat 5.5 Statistical Package for Windows, Unistat Ltd., London, United Kingdom).

Homeostasis Model Assessment for Insulin Resistance: Insulin resistance as measured by the Homeostasis Model Assessment Insulin Resistance (HOMA IR) index correlates closely with insulin resistance as determined by euglycemic insulin clamp technique.[15,16] HOMA IR is calculated with the following formula:

HOMA IR = (fasting glucose mg/dl * fasting insulin μU/ml) / 22.5 * 18

Normal levels are considered <2.5.

Laparoscopic Adjustable Gastric Banding: Our surgical technique for LAGB has been detailed previously.[17] In brief, we use the pars flaccida technique popularized by O'Brien and Fielding.[18-20] The adjustable band (Lap-Band®, Inamed, Allergan, Santa Barbara, CA) is locked in position around the stomach and secured in position with three sutures. The reservoir is placed on the mid-line approximately half way between the xyphoid and umbilicus. The patients are maintained on a liquid diet for 2 weeks after surgery and then on a soft diet for another 2 weeks. The first fill is not given until at least 2 months after surgery.

Laparoscopic Roux-en-Y Gastric Bypass: We have detailed our technique for LRYGBP previously.[21,22] Briefly, a lesser curve based pouch is separated from the remainder of the stomach. A stapled jejuno-jejunostomy is constructed 40 cm beyond the ligament of Trietz. The Roux limb is 100 cm long and is passed in a retro-colic, ante-gastric fashion. A two-layered hand-sewn gastro-jejunostomy is fashioned with absorbable sutures. Patients remain on a liquid diet for 2 weeks after surgery and on a soft diet for another 2 weeks.

Results

Demographics: The 56 LAGB patients had a median age of 41.6 years (25.7-63.0 years) and body mass index (BMI) of 45.5 kg/m^2 (25.0-66.0 kg/m^2) (Table 1). The 61 LRYGBP patients had a median age of 39.9 years (22.1-64.2 years) and BMI of 45.0 kg/m^2 (36.0-62.0 kg/m^2). There were no significant differences in age, height, weight or BMI between the LAGB and LRYGBP patients. Sex distribution was similar for both groups: LAGB 75% female and LRYGBP 79% female (Table 2). Racial and ethnic distribution of patients was similar for both groups (Table 2). There were no Oriental or Native American patients.

Table 1. Age (years), height (cm), weight (kg) and BMI (kg/m^2) for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. There are no significant differences between groups by ANOVA

LAGB	Age (yrs)	Ht (cm)	Wt (kg)	BMI (kg/m^2)
N	56	00	56	56
Median	42.5	00	128.6	45.5
Minimum	25.7	00	83.2	35.0
Maximum	63.0	00	216.8	66.0
LRYGP	**Age (yrs)**	**Ht (cm)**	**Wt (kg)**	**BMI (kg/m^2)**
N	61	00	61	61
Median	39.9	00	125.5	45.0
Minimum	22.1	00	94.1	36.0
Maximum	64.3	00	185.5	62.0

Type 2 Diabetes Mellitus and Co-Morbid Illnesses: Among the 56 LAGB patients, 42.9% manifested clinical T2DM (Table 3). Only 8 of these patients used oral diabetes medications and none required insulin before surgery. Among the 61 LRYGBP patients, 44.3% exhibited clinical T2DM. Ten of these patients used oral medications and one required insulin preoperatively. Rates of T2DM, use of oral

Table 2. Sex, race and ethnicity for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. There were no significant differences between groups by chi-square

LRYGBP	N	%	LAGB	N	%
Female	48	78.7%	Female	42	75%
Male	13	21.3%	Male	14	25%
White	48	78.7%	White	45	80.4%
Black	13	21.3%	Black	11	19.6%
Non-Hispanic	51	83.6%	Non-Hispanic	47	83.9%
Hispanic	10	16.4%	Hispanic	9	16.1%

Table 3. Status of type 2 diabetes mellitus (T2DM) for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. There were no significant differences between the groups by chi-square

LAGB	N	%	LRYGBP	N	%
No T2DM	32	57.1%	No T2DM	34	55.7%
T2DM	24	42.9%	T2DM	27	44.3%
No Oral Meds	48	85.7%	No Meds	51	83.6%
1 Oral Med	4	7.1%	1 Oral Med	6	9.8%
2 Oral Meds	3	5.4%	2 Oral Meds	2	3.9%
3 Oral Meds	1	1.8%	3 Oral Meds	2	3.9%
No Insulin	56	100.0%	No Insulin	60	984 %
Insulin	0	0.00%	Insulin	1	1.6%

medications and insulin dependence were similar for both groups of patients. There were no patients with type 1 diabetes mellitus. The rates of co-morbid diseases are listed in Table 4. There were no significant differences in the distribution of co-morbid diseases between LAGB and LRYGBP patients.

Weight Loss Following Surgery: LAGB patients were seen a median of 45 days (18-90 days) after surgery and LRYGBP patients 46 days (8-88 days) (Table 5). BMI dropped significantly less for the LAGB patients (4 kg/m^2) than in the LRYGBP patients (6 kg/m^2). Similarly, change in weight and % excess weight loss (%EWL) were significantly greater in the LRYGBP patients (Table 5).

Table 4. Co-morbid conditions for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. There were no significant differences between the groups by chi-square

	LAGB		LRYGBP	
	N	%	N	%
Asthma	8	14.3%	14	23.0%
Sleep Apnea	18	32.1%	24	39.3%
Hypertension	19	33.9%	22	36.1%
Coronary Artery Dx	2	3.6%	1	1.6%
Hypercholesterolemia	28	50.0%	31	50.8%
Hypertriglyceridemia	22	39.3%	20	32.8%
GERD	26	46.4%	35	57.4%
Urinary Stress Incont	22	39.3%	18	29.5%
Hx of Depression	28	50.0%	36	59.0%

Glucose, Insulin and Hemoglobin A1c: Preoperative and postoperative fasting glucose, fasting insulin and hemoglobin A1c levels are listed in Table 6 for both groups. Only the postoperative serum insulin levels significantly differed: LAGB patients 12.3 and LRYGBP patients 9.1.

Preoperative and Postoperative HOMA IR: Preoperative HOMA IR indices were similar for both groups (Table 7). Postoperative HOMA IR dropped significantly for both groups. Although the postoperative HOMA IR was significantly lower for the LRYGBP patients (LAGB 2.6 versus LRYGBP 2.2), the change in HOMA IR was similar following LRYGBP and LAGB. When patients were stratified for presence or absence of clinical T2DM, there was a significant drop in HOMA IR for both LAGB and LRYGBP patients. The change in HOMA IR was significantly greater, however, for both LRYGBP groups when compared to the non-diabetic LAGB patients but not the diabetic LAGB patients (Table 8). When changes in HOMA IR values were stratified by months of follow-up after surgery, there were no significant differences between the two groups (Table 9). Change in HOMA IR did not significantly correlate with number of days of follow-up (Figure 1), weight loss, drop in BMI or %EWL for either group. Interestingly, change in HOMA IR strongly correlated with preoperative HOMA IR indices for both groups, and there was no significant difference between the slopes or intercepts for the two regression lines (Figure 2). The regression line for LAGB was: Δ HOMA IR = 0.94*(Preoperative HOMA IR) – 3.3 (correlation coefficient r 0.8263, $P<0.0001$). The regression for LRYGB was: Δ HOMA IR = 0.90*(Preoperative HOMA IR) – 2.0 (correlation coefficient r 0.9711; $P<0.00001$).

Discussion

In this study, we compared changes in insulin resistance during the first 90 days following a total of 117 bariatric operations: 56 LAGBs and 61 laparoscopic short-limb Roux-en-Y gastric bypasses. The demographics, BMIs, presence of T2DM and rates of other co-morbid conditions were similar for the 56 LAGB patients and 61 LRYGBP patients. There

Table 5. Number of days following surgery on which postoperative values were obtained, follow-up weight (kg), change in weight (kg), follow-up BMI (kg/m²) and %EWL for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. * indicates significant differences between groups by ANOVA (*P*<0.05)

LAGB	Days F/U	F/U Wt (kg)	Δ Wt (kg)	F/U BMI (kg/m²)	Δ BMI (kg/m²)	% EWL
N	56	56	56	56	56	56
Median	45	118.4*	10.0*	42.0	4.0*	14.8%*
Minimum	18	78.4	4.1	32.6	1.0	6.9%
Maximum	90	196.4	32.7	63.0	10.0	37.0%
LRYGBP	**Days F/U**	**F/U Wt kg)**	**Δ Wt (kg)**	**F/U BMI (kg/m²)**	**Δ BMI (kg/m²)**	**%EWL**
N	61	61	61	61	61	61
Median	46	111.4*	15.9*	41.0	6.0*	24.1%*
Minimum	8	69.1	5.9	24.0	2.0	9.8%
Maximum	88	158.2	28.2	55.0	17.0	51.4%

Table 6. Preoperative and postoperative fasting serum glucose, insulin and hemogloblin A1c levels for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. * indicates significant differences between groups by ANOVA (*P*<0.05)

LAGB	Preop Glucose mg/dl	Postop Glucose mg/dl	Preop Insulin μU/ml	Postop Insulin μU/ml	Preop HgbA1c	Postop HgbA1c
N	56	56	56	56	54	54
Median	95.0	90.0	16.4	12.3*	5.7	5.5
Minimum	76.0	71.0	7.3	3.6	4.8	4.6
Maximum	331.0	168.0	137.0	100.0	12.2	8.3
LRYGBP	**Preop Glucose mg/dl**	**Postop Glucose mg/dl**	**Preop Insulin μU/ml**	**Postop Insulin μU/ml**	**Preop HgbA1c**	**Postop HgbA1c**
N	61	61	61	61	61	58
Median	97.0	91.0	17.7	9.1*	5.8	5.4
Minimum	77.0	58.0	2.7	3.8	4.3	4.3
Maximum	261.0	141.0	128.0	49.0	12.3	8.2

were no significant differences between the preoperative fasting glucose, insulin and hemoglobin A1c levels. Duration of follow-up for the two groups was also similar: LAGB 45 days (18-90 days) and LRYGBP 46 days (8-88 days). Following surgery, LAGB patients achieved significantly less %EWL: LAGB 14.8% (6.9 %-37.0 %) and LRYGBP 24.1% (9.8%-51.4%). Although postoperative HOMA IR levels were significantly lower in the LRYGBP patients, 2.2 (0.7-12.2), than in the LAGB patients, 2.6 (0.8-29.6), the change in HOMA IR was similar for both groups. Similarly, there was no significant difference in the drop in HOMA IR between the two groups during the first, second or third month following surgery. Preoperative HOMA IR was a much more important predictor of change in HOMA IR than the type of surgery performed on the patient. This study indicates that both LAGB and LRYGBP significantly improve insulin resistance as measured by HOMA IR in the first 90 days following surgery.

Several studies have examined changes in insulin resistance following LAGB. Phillips and colleagues[23] studied 10 non-diabetic patients 3 months following LAGB. Their HOMA IR did not significantly change: preoperative HOMA IR 2.2 (1.3-3.1) and postoperative HOMA IR 3.2 (0.9-4.7). Their BMI dropped from 41 kg/m^2 (33-47 kg/m^2) to 36 kg/m^2 (29-41 kg/m^2). In contrast, the 1.0 drop

Table 7. Preoperative and postoperative Homeostasis Model Assessment for Insulin Resistance (HOMA IR) for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. * # + indicate significant differences between groups by ANOVA (*P*<0.05)

LAGB	Preop HOMA IR	Postop HOMA IR	Δ HOMA IR
N	56	56	56
Median	4.1+	2.6 + *	1.4
Minimum	1.4	0.8	-26.4
Maximum	39.2	29.6	34.4
LRYGBP	**Preop Insulin**	**Postop HOMA IR**	**HOMA IR**
N	61	61	61
Median	5.0#	2.2# *	2.6
Minimum	0.6	0.7	-1.4
Maximum	56.5	12.2	53.9

(Table 8) in HOMA IR for our non-diabetic LAGB patients was statistically significant, perhaps because of a larger sample size. Other groups have reported changes in HOMA IR 1 year following LAGB. Pontiroli and colleagues[24] found that the HOMA IR dropped from 5.1 ± 0.28 to 2.5 ± 0.14 in 143 LAGB patients one year after surgery. BMI for these patients dropped from 44.9 ± 0.53 kg/m^2 to 36.9 ± 0.46 kg/m^2. Gazzaruso and colleagues[25] also found a significant drop in HOMA IR 1 year following LAGB: preoperative HOMA IR 4.2 ± 2.0 and postoperative HOMA IR 2.4 ± 1.0.24 The BMI of their 51 patients dropped from 43.3 ± 6.9 kg/m^2 to 34.5 ± 7.4 kg/m^2. Preoperative and postoperative values in these two studies are similar to our findings within the first 3 months following surgery (Table 7) even though their reported drop in BMI was greater. Since LAGB restricts food intake, our findings support the concept that the caloric restriction imposed by LAGB plays an important role in improving insulin resistance.

Table 8. Change in HOMA IR for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. Patients are also stratified by the presence or absence of clinical Type 2 Diabetes Mellitus (T2DM). * and ** indicate significant differences between groups by ANOVA (*P*<0.05)

Δ HOMA IR	LAGB No T2DM	LAGB T2DM	LRYGBP No T2DM	LRYGBP T2DM
N	32	24	34	27
Median	1.0* **	3.9	2.2*	3.6**
Minimum	-26.4	-5.5	-1.4	-0.6
Maximum	14.5	34.4	53.9	38.8

Insulin resistance also improves following gastric bypass surgery. Pories' group[26] reported a significant drop in HOMA IR 1 year following RYGBP. Preoperative HOMA IR plummeted from 7.0 ± 1.9 to 0.5 ± 0.1 1 year following surgery in six patients.25 BMI decreased from 52.2 ± 2.5 kg/m^2 to 27.9 ± 0.8 kg/m^2. Papapietro and colleagues[27] reported that HOMA IR dropped in 232 RYGBP patients from 11.7 ± 7 to 2.2 ± 2 3 months after surgery, 1.9 ± 1 6 months after surgery and 1.45 ± 0 1 year after surgery. T2DM was present in 40 of these 232 patients (17.3%). BMI for these patients decreased from 44 ± 6 kg/m^2 to 29.3 ± 4 kg/m^2 1 year postoperatively. Stubbs's group[9] examined changes in HOMA IR in 71 patients following gastric bypass. Mean HOMA IR for non-diabetic patients 6 days after RYGBP was 1.29, for impaired glucose tolerance patients 1.95 and for T2DM patients 3.67. These values are strikingly close to the values for our non-diabetic and T2DM patients for the 3 months after both LAGB and LRYGBP. These studies indicate that HOMA IR drops rapidly after gastric bypass surgery and remains at this low level for at least 1 year after surgery.

Previous studies have not directly compared changes in HOMA IR in two similar groups of patients who underwent different types of bariatric operation. In our study, LRYGBP achieved significantly greater %EWL within 90 days of surgery than LAGB (Table 5) and significantly lower HOMA IR levels; yet the change in HOMA IR did not achieve statistical significance (Table 7). Interestingly, change in postoperative HOMA IR did not correlate with number of days following surgery for either LRYGBP or LAGB (Figure 1). Similarly, change in HOMA IR was not significantly different between 1, 2 or 3 months of follow-up for either operation (Table 9). Consequently, our study suggests that a common mechanism present following both LAGB and LRYGBP, such as calorie restriction, mediates much of the improvement in

Table 9. %EWL and change in HOMA IR for 56 patients who underwent LAGB and 61 patients who underwent LRYGBP. Values are also stratified into three groups by number of days of follow-up when the values were obtained. * indicates significant differences between groups by ANOVA (*P*<0.05)

1-30 Days LAGB	%EWL	Δ HOMA IR	1-30 Days LRYGBP	%EWL	Δ HOMA IR
N	10	10	N	14	14
Median	13.1%	0.9	Median	19.3%	3.6
Minimum	7.3%	-4.0	Minimum	9.8%	-1.4
Maximum	30.9%	18.2	Maximum	25.9%	53.9
31-60 Days LAGB	**%EWL**	**Δ HOMA IR**	**31-60 Days LRYGBP**	**%EWL**	**Δ HOMA IR**
N	30	30	N	34	34
Median	14.3%*	1.5	Median	24.0%*	2.5
Minimum	7.9%	-5.5	Minimum	15.1%	-0.7
Maximum	29.1%	34.4	Maximum	51.4%	15.6
61-90 Days LAGB	**%EWL**	**Δ HOMA IR**	**61-90 Days LRYGBP**	**%EWL**	**Δ HOMA IR**
N	16	16	N	13	13
Median	19.5%*	1.3	Median	29.7%*	2.7
Minimum	6.9%	-26.4	Minimum	21.8%	0.2
Maximum	37.0%	14.7	Maximum	47.1%	19.8

insulin resistance following both operations. In addition, our data suggest that a second mechanism such as alterations in the entero-insular axis or superior weight loss may augment the improvement in insulin resistance following LRYGBP.

The best predictor of postoperative change in HOMA IR for both groups of patients in this study was the preoperative HOMA IR (Figure 2; correlation coefficient r for LAGB 0.8263 and LRYGBP 0.9711). Increased preoperative insulin resistance leads to increased postoperative drop in HOMA IR. As shown in Figure 2, the regression line for both operations was remarkably similar. The clinical correlate of this is shown in Table 8: drop in HOMA IR was greater for patients with T2DM than non-diabetic patients. This

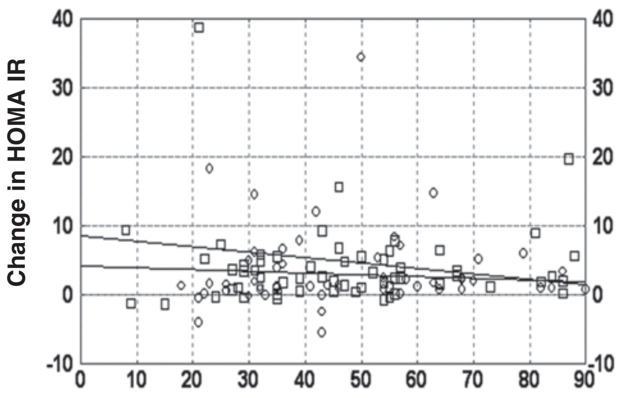

Figure 1. Number of days following surgery on which values were obtained (Days of Follow-up) and change in HOMA IR for 56 patients who underwent LAGB (Circles) and 61 patients who underwent LRYGBP (Squares). There was no significant difference between the first degree regressions by heterogeneity of regression test.

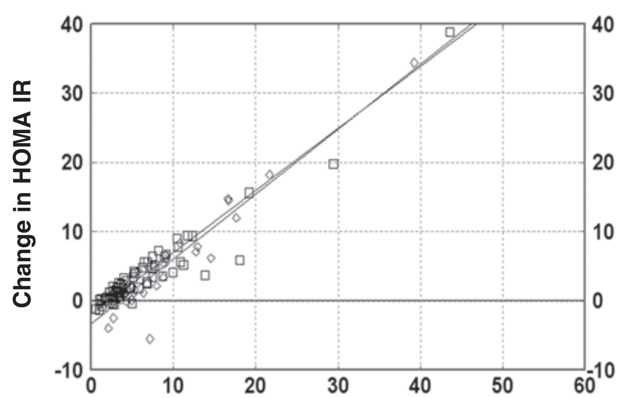

Figure 2. Preoperative HOMA IR and change in HOMA IR for 56 patients who underwent LAGB (Diamonds) and 61 patients who underwent LRYGBP (Squares). There was no significant difference between the first degree regressions for the two groups by heterogeneity of regression test.

strongly suggests that much of the improvement in insulin resistance following both LAGB and LRYGBP is mediated by a common mechanism: one that determines the similar regression lines shown in Figure 2. As suggested previously, restricted caloric intake seems a likely putative mechanism.[1,28]

Postoperative HOMA IR levels were significantly lower following LRYGBP than after LAGB (Table 7). This suggests that an additional mechanism may contribute to changes in insulin resistance following LRYGBP that does not contribute to changes observed after LAGB. Following LRYGBP, nutrients bypass much of the foregut resulting in significant changes in the postprandial release of gut hormones that participate in the entero-insular axis.[11] Rubino, first in conjunction with Gagner's group[12] and more recently with Marescaux's group,[13] has generated both clinical and experimental data to support this hypothesis. Rubino first studied changes in glucose and insulin 3 weeks following LRYGBP in 10 patients. Surgery precipitated significant improvements in glucose and insulin metabolism before significant weight loss occurred.[12] In animal studies, Rubino and colleagues[13] performed sham operations or constructed gastro-jejunal bypasses in non-obese rats afflicted with an animal model of T2DM. Both groups received identical diets in terms of calories following surgery. Rats following gastro-jejunal bypass experienced a significant improvement in glucose tolerance. These authors concluded that "Our study pinpoints the exclusion of the duodenum-jejunum as the factor responsible for the control of diabetes" following gastric bypass. Our study also supports a role of alterations in the entero-insular axis in the improvement in glucose and insulin metabolism following gastric bypass surgery for morbid obesity.

Weight loss may also mediate changes in insulin resistance following bariatric surgery. Weight, BMI and %EWL all significantly dropped in our patients throughout the study period. Yet, postoperative HOMA IR indices and change in HOMA IR indices did not correlate with weight loss, change in BMI or %EWL. In contrast, Scopinaro's group studied 36 non-diabetic patients 2 years after biliopancreatic diversion (BPD).[29] Their BMIs dropped from preoperative levels of 44.6 ± 5.6 kg/m^2 to 28.3 ± 3.5 kg/m^2. The drop in BMI was similar at 1 and 2 years after BPD. Their HOMA IR dropped from 4.13 ± 2.95 to 0.91 ± 0.35 2 years after surgery. These authors concluded that the stable weight loss following BPD was accompanied by "complete reversal of the preoperative insulin resistance". In a long-term study of patients afflicted with T2DM, Scopinaro's group reached similar conclusions.[14] Clinical improvement in T2DM was studied in 312 T2DM patients 10 years after undergoing BPD. The BMI in these patients dropped from 50.1 ± 9.0 kg/m^2 before BPD to 32.0 ± 6.7 kg/m^2 10 years after BPD. Clinical resolution of T2DM was observed in 189 of 195 patients 10 years after surgery. Our study did not address the role of weight loss in modulating insulin resistance, probably because we limited our observations to the first 90 days following surgery.

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