Health Outcomes of Severely Obese Type 2 Diabetic Subjects 1 Year After Laparoscopic Adjustable Gastric Banding

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OBJECTIVE — To prospectively examine the effect of weight loss 1 year after laparoscopic adjustable gastric band surgery on a broad range of health outcomes in 50 diabetic subjects.

RESEARCH DESIGN AND METHODS — A total of 50 (17 men, 33 women) of 51 patients with type 2 diabetes, from a total of 500 consecutive patients, were studied preoperatively and again 1 year after surgery.

RESULTS — Preoperative weight and BMI (means ± SD) were 137 ± 30 kg and 48.2 ± 8 kg/m^2, respectively; at 1 year, weight and BMI were 110 ± 24 kg and 38.7 ± 6 kg/m^2, respectively. There was significant improvement in all measures of glucose metabolism. Remission of diabetes occurred in 32 patients (64%), and major improvement of glucose control occurred in 13 patients (26%); glucose metabolism was unchanged in 5 patients (10%). HbA_{1c} was 7.8 ± 3.2% preoperatively and 6.2 ± 2.7% at 1 year ($P < 0.001$). Remission of diabetes was predicted by greater weight loss and a shorter history of diabetes (pseudo $r^2 = 0.44$, $P < 0.001$). Improvement in diabetes was related to increased insulin sensitivity and β-cell function. Weight loss was associated with significant improvements in fasting triglyceride level, HDL cholesterol level, hypertension, sleep, depression, appearance evaluation, and health-related quality of life. Early complications occurred in 6% of patients (wound infections in 4%, respiratory support in 2%), and late complications occurred in 30% of patients (gastric prolapse in 20%, band erosion in 6%, and tubing leaks in 4%). All late complications were successfully revised surgically.

CONCLUSIONS — Modern laparoscopic weight-loss surgery is effective in managing the broad range of health problems experienced by severely obese individuals with type 2 diabetes. Surgery should be considered as an early intervention.

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There is an epidemic of obesity throughout most of the developed and much of the developing world. The prevalence of obesity (BMI >30 kg/m^2) has doubled in most Western countries in the last 15–20 years. Obesity is a major independent risk factor for the development of type 2 diabetes (1) and is associated with the rapid increase in the prevalence of type 2 diabetes (2). A total of 80% of individuals with type 2 diabetes are obese (3). The risk of developing type 2 diabetes increases with the degree of obesity, duration of obesity, central weight distribution, and weight gain during adult life (4). A decrease in insulin sensitivity with increasing obesity, especially central obesity, is associated with impaired glucose tolerance, dyslipidemia, and systemic hypertension, all of which are features of the metabolic syndrome and are associated with cardiovascular risk.

Early intensive treatment of type 2 diabetes and its associated vascular risk factors reduces morbidity, mortality, and poor quality of life associated with long-term macrovascular and microvascular complications (5,6). Early intensive therapy may also delay the progressive deterioration of β-cell function, a characteristic of type 2 diabetes. Type 2 diabetes is a progressive disease, and with loss of β-cell function, it requires increasing treatment over time to maintain control.

The beneficial effect of weight reduction on control of type 2 diabetes has been known for some time (7). Studies have shown benefit from modest weight reduction (8). However, even modest weight reductions have been difficult to achieve and maintain with nonsurgical methods of weight loss. Optimal and continuous application of a combination of dietary and drug therapy in association with increased exercise and behavioral modification can, at best, achieve and maintain a 5–10% loss of body weight. For severely obese individuals, this is insufficient to solve the problem. Perhaps the most dramatic effect of weight loss on type 2 diabetes has been reported after gastric bypass surgery. Weight loss after gastric bypass surgery in severely obese individuals (BMI >35 kg/m^2) prevents the development of type 2 diabetes (9) and leads to resolution of abnormal glucose tolerance in most patients with type 2 diabetes (10). This effect reduces long-term mortality (11). It has been hypothesized that bypass of the duodenum may provide a specific advantage with gastric bypass (12). The benefit of weight loss has also been demonstrated after gastric restrictive surgery.

The option of major invasive surgery, with irreversible change in the anatomy of the gut and significant perioperative risk, is being sought by very few individuals. It is estimated that ~30,000 major bariatric procedures are performed each year in the U.S. This represents only 1 in every 400 of the 12 million severely obese individuals. The recent introduction of a laparoscopi-

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Abbreviations: %EWL, percentage of excess weight loss; %EWL1, %EWL at 1 year; HOMA, homeostasis model assessment; HUMA%B, percentage of β–islet cell function assessed by HOMA; HOMA%S, percentage of insulin sensitivy assessed by HOMA; LAGB, laparoscopically placed adjustable gastric band; pr^2, pseudo r^2.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

cally placed adjustable gastric band (LAGB; Lap-Band System; BioEnterics, Carpinteria, CA) is potentially a more acceptable option for individuals with severe obesity who do not wish to consider the more invasive, nonadjustable, and essentially irreversible alternative of gastric bypass.

The Lap-Band System consists of a band of silicone elastomer with an inflatable inner shell and a buckle closure connected by tubing to an access port placed outside the abdominal cavity. The inner diameter of the band can be readily adjusted by the addition or removal of saline through the access port. The band is placed laparoscopically around the upper stomach, ~1 cm below the esophagogastric junction.

We have been using the Lap-Band System as the primary modality of treatment for severe obesity since 1994. The aim of this study was to prospectively examine the effect of weight loss 1 year after surgery on a broad range of health outcomes in 50 consecutive patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS

Patients with BMI >35 kg/m^2 with significant medical, physical, or psychosocial disabilities and who had attempted weight reduction by other means for ≥5 years were considered for entry into the study. After two consultations with the surgeon, during which the clinical evaluation was completed and the procedure was discussed extensively, patients who elected to proceed underwent extensive preoperative assessment. This included clinical assessment by a consultant physician and endocrinologist, anthropometric measurements, and laboratory tests. All patients were screened for diabetes, and a careful history of diabetes, risk factors for diabetes, and comorbidities associated with diabetes were recorded. Informed written consent was obtained from all patients, and the study was conducted in conformance with the Helsinki Declaration.

The study group consisted of patients with diabetes who underwent the procedure between November 1996 and November 1999. During this time 500 patients underwent insertion of the Lap-Band System; of these 500 patients, 51 (10%) had type 2 diabetes.

Laboratory tests included fasting lipid profile (which included total cholesterol, fasting triglyceride, and HDL cholesterol, with LDL cholesterol calculated from these if the fasting triglyceride was <4.6 mmol/l), fasting plasma glucose, fasting plasma insulin, C-peptide, HbA_{1c}, and liver function tests. These assays were performed in an approved laboratory with internal and external quality control.

Diagnosis of type 2 diabetes was based on the American Diabetes Association criteria. Hypertension was diagnosed if the patient had a history of hypertension and was taking antihypertensive medication or if the patient had a resting recumbent blood pressure of ≥140/90 mmHg on at least two occasions. Health-related quality of life was assessed using the Medical Outcomes Trust SF-36 (Boston, MA) (13,14), depression was assessed with the Beck depression inventory, and appearance was assessed using the multidimensional body self-relations questionnaire (15). Sleep was assessed using a standard questionnaire for sleep symptoms (16), and the Epworth sleepiness scale was used to asses daytime sleepiness (17). Weight loss is expressed as percentage of excess weight loss (%EWL), a standard method for reporting results of weight-loss surgery. Preoperative excess weight is calculated as weight (in kg) at the time of surgery minus ideal weight (in kg), as measured by the Metropolitan Life tables. %EWL at 1 year (%EWL1) is calculated by dividing the weight change at 12 months by the excess weight preoperatively multiplied by 100.

Insulin sensitivity and β-cell function

Insulin levels were measured using an immunoenzymometric assay (MEIA; Abbott Diagnostics, North Chicago, IL) with interassay and intra-assay coefficients of variation <3%. C-peptide was measured using a double-antibody competitive radioimmunoassay with interassay and intra-assay coefficients of variation <7%.

A validated method of estimating insulin resistance and β–islet cell function using the fasting plasma glucose and C-peptide measures (homeostasis model assessment [HOMA]) was used to calculate percentage of insulin sensitivity (HOMA%S) and the percentage of β–islet-cell function (HOMA%B). This homeostasis model assessment (HOMA) was developed by Matthews and later modified. This method has been validated in subjects with type 2 diabetes and obesity (18).

Data analysis

Variables were assessed for correlation using nonparametric bivariate analysis. Two samples of quantitative variables were tested by two-sided Student's *t* test (mean ± SD) or by Mann-Whitney *U* test (median ([interquartile range]). Some quantitative laboratory variables, e.g., fasting plasma insulin, required log transformation before parametric analysis. The χ^2 method (Fisher's exact test) was used to test the significance of differences between proportions and categorical variables. Multivariate analysis was tested using binary logistic regression (forward and backward) and linear regression analysis. A P value <0.05 was considered statistically significant. No correction was used for assessing correlation with multiple variables. The statistical software SPSS for Windows (version 10.0.5; SPSS, Chicago, IL) was used for analysis.

RESULTS

Of the 500 consecutive patients presenting for Lap-Band System surgery, 51 patients had type 2 diabetes. One patient emigrated soon after band placement and was lost to follow-up. Therefore, 50 patients (17 men, 33 women) were followed in this study. Preoperative weight and BMI (mean ± SD) were 137 ± 30 kg and 48.2 ± 8 kg/m^2, respectively; at 1 year, weight and BMI were 110 ± 24 kg and 38.7 ± 6 kg/m^2, respectively. The %EWL1 was 38 ± 14%, significantly less than 47 ± 17% (P = 0.01) for the cohort of 500.

Lap-Band System surgery

Laparoscopic placement of the Lap-Band System adjustable gastric band was achieved in 47 patients, and there were no intraoperative conversions to an open procedure. The remaining three patients underwent elective open placement of the band because they were undergoing revisional surgery for weight gain after gastroplasty. The median hospital stay for laparoscopic placement is 2 days.

Weight loss is progressive over the first 2–3 years and plateaus at 6 years; after 2 years, the mean excess weight loss is 50–60%. In our group of 50 patients, there were three early complications. Two patients had wound infections and one patient required postoperative respiratory support; all of these complications oc-

Table 1—*Changes in measures of glucose metabolism, lipids, liver function, and the number of subjects using medication for diabetes, for 50 diabetic patients before and 1 year after LAGB weight-loss surgery*

	Reference range	Pre–LAGB	1 Year	*P*
Glucose metabolism				
Fasting plasma glucose (mmol/l)*	3.6–5.5	9.4 ± 3.3	6.2 ± 2.7	<0.001
HbA_{1c} (%)*	4.3–6.1	7.8 ± 3.2	6.2 ± 1.5	<0.001
Fasting plasma insulin (pmol/l)*	12–120	132 ± 96	84 ± 60	0.001
C-peptide (nmol/l)*	260–1,320	1,470 ± 760	1,030 ± 650	<0.001
HOMA%S*		25 ± 12	39 ± 33	<0.001
HOMA%B*		78 ± 79	119 ± 77	0.001
Lipids				
Cholesterol (mmol/l)†	2.9–5.5	5.74 ± 1.1	5.57 ± 1.0	0.50
Fasting triglyceride (mmol/l)*	0.2–2.0	2.43 ± 1.6	1.39 ± 0.7	<0.001
HDL cholesterol (mmol/l)†	1.0–2.9	1.03 ± 0.3	1.22 ± 0.3	0.04
LDL cholesterol (mmol/l)†	1.7–3.5	3.45 ± 0.8	3.67 ± 0.9	0.30
Cholesterol–to–HDL cholesterol ratio†	1.0–4.0	6.00 ± 1.8	4.80 ± 1.40	0.008
Liver enzymes				
Alanine aminotransferase (IU/l)*	0–40	37.2 ± 32	19.3 ± 11	<0.001
Aspartate aminotransferase (IU/l)*	5–34	27.8 ± 23	17.1 ± 7	0.002
γ-glutamyl transferase (IU/l)*	0–50	50.7 ± 30	25.3 ± 14	<0.001
Medication				
Insulin‡	—	4 (8)	4 (8)	NS
Oral hypoglycemic‡	—	29 (58)	8 (16)	<0.001

Data are means ± SD and *n* (%), unless otherwise indicated. *Wilcoxon sign-geometric mean (interquartile range); †paired-samples Student's *t* test mean (SD); ‡χ^2.

curred after open surgery. The most significant late postoperative problem is prolapse of the stomach through the band (n = 10 [20%]), which requires laparoscopic revision. In three patients (6%), erosion of the band into the stomach occurred, requiring removal of the band, repair of the gastric defect, and replacement of the band. In two patients (4%), tubing leaks required minor surgical correction. Late complications include all complications for the 50 subjects postoperatively, not only those occurring in the first year.

Impact on diabetes

Weight loss had a major impact on diabetes. The changes in measure of glucose metabolism, insulin resistance, and β-cell function are shown in Table 1. At 1 year of follow-up, the group had geometric mean fasting glucose levels in the nondiabetic range, and mean insulin and C-peptide levels were normal. There was also a major reduction in the use of oral hypoglycemic medication (Table 1). Four patients were on insulin therapy before the surgery. At 1 year, all four patients remained on insulin therapy; however, in three of these patients, the dose of insulin had been reduced markedly and glycemic control had improved, and in one patient, insulin therapy was unchanged. Remission of diabetes, as defined by normal fasting plasma glucose, HbA_{1c}, fasting insulin, and C-peptide, occurred in 32 patients (64%). Major improvement in glycemic control occurred in 13 patients (26%), and in 5 patients (10%), glycemic control was unchanged. Only three patients had a HbA_{1c} level >7% at 1-year review.

Remission of diabetes, improvement in glycemic control, and no change were scored as 2, 1, and 0, respectively. Using ordinal logistic regression analysis, four factors were found to significantly predict remission of diabetes: greater %EWL1 (pseudo r^2 Cox and Snell [pr^2] = 0.37, $P < 0.001$), shorter duration of diabetes (pr^2 = 0.24, $P = 0.003$), better preoperative β-cell function (pr^2 = 0.11, P = 0.034), and lower preoperative fasting plasma glucose level (pr^2 = 0.17, P = 0.012). The last two factors were not significant after controlling for duration of diabetes. The two remaining factors had significant independent effects, with %EWL1 positively associated with remission and duration of diabetes negatively associated with remission, with a combined pr^2 = 0.44, $P < 0.001$.

All patients undergo yearly fasting plasma glucose as screening for diabetes, and <2% of patients are currently lost to follow-up. However, not all patients are seen in the window period of annual follow-up. We have followed 434 nondiabetic subjects at 1 year, 255 at 2 years, 144 at 3 years, and 90 at ≥4 years. For an accumulated 923 patient-years, none of the nondiabetic individuals has developed diabetes. In all, 67 patients have presented with impaired fasting glucose (6.1–6.9 mmol/l). A total of 57 patients have been followed for at least 1 year, 30 for 2 years, 17 for 3 years, and 10 for ≥4 years (114 patient-years). Of the 57 patients followed for at least 1 year, 6 had impaired fasting glucose at 1 year, and none of the patients followed for ≥2 years had impaired fasting glucose. These data are consistent with a reduced risk of developing type 2 diabetes after weight-loss surgery.

Insulin sensitivity and β-cell function

Insulin sensitivity and β-cell function both improved significantly with weight

Table 2—Health-related quality of life (SF-36) scores presurgery and at 1 year follow-up and comparison with healthy community levels

	Presurgery	1 Year	P*	Community levels
n	35	35		
Physical function	38 ± 24	77 ± 25	<0.001	88
Physical role	42 ± 39	84 ± 30	<0.001	83
Pain	61 ± 27	84 ± 21	<0.001	74
General health	35 ± 25	72 ± 22	<0.001	74
Energy	30 ± 23	61 ± 24	<0.001	59
Social function	58 ± 34	78 ± 23	0.012	83
Emotional role	55 ± 43	71 ± 35	0.14	80
Mental health	58 ± 26	73 ± 20	0.014	73

Data are means ± SD, unless otherwise indicated. *Paired Student's t test (two-sided).

loss (Table 1). Improved insulin sensitivity (as measured by HOMA%S) was best predicted by the %EWL1 ($r = 0.47$, $P = 0.005$). β-Cell function improves with weight loss, but the change did not correlate with the %EWL1 ($r = 0.05$, $P = 0.7$). There was a negative trend between the change in β-cell function and the length of time with a diagnosis of diabetes ($r = -0.29$, $P = 0.1$). The β-cell function preoperatively did not correlate well with a history of diabetes ($r = -0.19$, $P = 0.3$); however, after 1 year of weight loss and the associated improvement in insulin sensitivity, there was a significant negative correlation ($r = -0.46$, $P = 0.008$) after controlling for sex, age, and presenting BMI.

Dyslipidemia

Significant improvement in the dyslipidemia of obesity and diabetes occurred with weight loss (Table 1). There was a 43% decrease in mean fasting triglyceride and a 20% decrease in the mean total cholesterol/HDL cholesterol ratio, with an 18% increase in mean HDL cholesterol levels. The %EWL1 did not have a significant effect on the decrease in triglyceride level ($r = -0.24$, $P = 0.14$). The %EWL1 was the only significant predictor of the increase in HDL cholesterol level ($r = 0.45$, $P = 0.03$).

Hypertension

Of the 50 subjects, 34 (68%) had a history of hypertension or were found to be hypertensive preoperatively. For patients with hypertension, the preoperative systolic and diastolic pressures (mean ± SD) were 154 ± 21 and 96 ± 14 mmHg, respectively, and at 1 year, the systolic and diastolic pressures were 130 ± 12 and 79 ± 13 mmHg, respectively ($P < 0.001$). Six patients (18%) were normotensive preoperatively and 24 patients (71%) were normotensive at 1-year follow-up (χ^2, $P < 0.001$). After 1 year, 7 patients (21%) had no change in hypertension, 12 patients (35%) had improved (normotensive but requiring antihypertensive medication), and 15 patients (44%) had resolved (normotensive and not on medication for hypertension).

Liver enzymes

Abnormal elevation of liver enzyme levels is commonly associated with obesity and diabetes. Geometric mean levels of alanine aminotransferase, aspartate aminotransferase, and γ-glutamyl transferase preoperatively and at 1 year are shown in Table 1. A total of 28 patients (56%) had at least one abnormally increased enzyme level preoperatively, and at 1 year, only 5 patients (10%) had at least one elevated enzyme level ($P < 0.001$).

Sleep disturbance

The most recent 35 operated patients in this study have completed sleep questionnaires as part of a larger study. Of these 35 subjects, 15 patients with diabetes who reported sleep apnea preoperatively reported resolution at 1 year. Patients also reported improved sleep quality ($P = 0.007$) and less daytime sleepiness (Epworth sleepiness scale, $P < 0.001$).

Depression/quality of life/appearance

The most recent 35 operated patients have also completed questionnaires related to depression, health-related quality of life, and appearance both preoperatively and at 1 year. There was improvement in the Beck depression inventory from 16.3 ± 6.5 to 9.6 ± 9 at 1 year ($P = 0.009$). The quality of life, as measured by SF-36, showed highly significant improvement in subscales related to physical health, and many of these subscales returned to normal values (Table 2). Of the 35 patients, 33 believed their health was unchanged or had deteriorated in the year before surgery. At follow-up, 34 of the 35 patients reported improvement in health during the past 12 months, and 1 patient reported no change in health. Significant improvement in the patients' evaluation of their appearance was noted at 1 year ($P = 0.007$).

CONCLUSIONS — This study confirms the major beneficial effects of weight loss in subjects with type 2 diabetes. In most of the subjects, diabetes remitted completely and 94% had excellent glycemic control. The change in glycemic control is a result of a change in the two fundamental features of type 2 diabetes: improvement in insulin sensitivity and improved β-cell function as measured indirectly by the homeostasis method (19).

Our study clearly shows that the percentage of excess weight lost and the duration of diabetes affect the likelihood of remission of type 2 diabetes. The improvement in insulin sensitivity is correlated with weight loss, but improvement in β-cell function is not. There is a tendency for β-cell function to improve more in those with a shorter duration of diabetes, and there is a highly significant relationship between post–weight-loss β-cell function and duration of diabetes. The above findings suggest that reversibility of β-cell dysfunction is variable and probably influenced by the duration of type 2 diabetes. Other studies have also variably reported the changes in β-cell function with weight loss (20,21).

Weight loss favorably changes other important cardiovascular risk factors in subjects with type 2 diabetes. Hypertension is better controlled; fewer patients require antihypertensive medication. These changes should reduce the risk of macrovascular and microvascular disease and reduce mortality (6). Optimal blood pressure control and long-term monitoring should remain a priority in these patients, because there is evidence that the effect of weight loss on hypertension may not be sustained (22). Favorable changes in lipids also accompany weight loss, with lower fasting triglyceride levels, higher HDL cholesterol levels, and improved total cholesterol–to–HDL cholesterol ratio. The size of LDL particles is the best indicator of coronary artery disease status, with small particles being highly atherogenic (23). The size of LDL particles is inversely related to BMI, fasting plasma insulin level, and fasting triglyceride level (24). Although LDL particle size was not measured in this study, the improved BMI, plasma insulin, and triglyceride concentration would suggest that LDL particle size may have also improved (increased).

The major predictors of nonalcoholic steatohepatitis in severely obese individuals (insulin resistance, systemic hypertension, and elevated aminotransferase levels) (25) are all favorably changed with weight loss.

Obese subjects with diabetes fail to lose the same amount of weight as those without diabetes. We have previously shown that reduced insulin sensitivity and the conditions associated with it are associated with a lower rate of weight loss after LAGB surgery (26). The reason for this is unknown but may relate to reduced energy expenditure in diabetic subjects or an effect of hyperinsulinemia on central control of energy balance, increasing appetite and, thus, energy intake.

Gastric bypass has a dramatic and rapid effect on type 2 diabetes in severely obese subjects; remission of diabetes is achieved in >80% of patients (10). Pories and Albrecht (27) have hypothesized that gastric bypass, with diversion of food from the duodenum, may have added benefit and proposed that the foregut may have an important role in the etiology of type 2 diabetes. The effect of bariatric surgery, both restrictive and diversionary, on insulin sensitivity, secretion, signaling, and pancreatic β-cell function requires further evaluation.

This follow-up study only reported changes at 1 year after surgery. We have demonstrated that the LAGB surgery is able to maintain weight for at least 6 years (28). Long-term studies after weight-loss surgery have shown that improvement in diabetes is maintained while weight loss is maintained (11,22). Weight gain throughout adult life is a significant risk factor for the development of diabetes (4). The absence of diabetes developing in any of our patients after surgery indicates that weight loss also protects against the development of diabetes, a finding common to other studies of weight loss (9,10).

Psychosocial stress and depression, which are common in severely obese subjects, have been linked to the development of diabetes and may have a common neuroendocrine basis (29). Our study demonstrates significant improvement in the Beck depression index, mental health and social function scale scores of the SF-36, and appearance evaluation, all of which are measures of improved psychosocial health. This is in association with the substantial improvement in physical ability, physical role, and energy and health perception, all of which are indicators of improved physical health.

The study does not contain a control group. In the past, a randomized comparison between surgical management of obesity, and optimal medical management for obese subjects with diabetes has been unacceptable because of the perceived invasiveness and dangers of gastric bypass and other open bariatric procedures. The small numbers of severely obese subjects seeking surgery in the past (estimated 1 in 400) is evidence of this. The availability of LAGB, a minimally invasive laparoscopic procedure that is safe, effective, easily adjustable, and completely reversible, should change this view. In the countries in which LAGB has been used widely, many patients accepting this surgery have previously rejected other surgical procedures. The results we present are attractive and present a dilemma to those looking after the severely obese patient with diabetes. Are current medical therapies really providing optimal care for this group? It is time for a randomized comparison of LAGB with continued optimal medical therapy as appropriate and a control group receiving optimal medical therapy. The Swedish obesity study, while not truly randomized, should provide some valuable data in this regard when results are finally released.

The evidence that early and intensive treatment of type 2 diabetes reduces morbidity, mortality, and poor quality of life (5,6) and may reduce the deterioration of β-cell function indicates that obesity surgery should be considered as an early intervention.

Except for the lack of randomized controlled data, no treatment of severely obese patients with diabetes is as broadly effective as weight-loss surgery. These patients should be considered for modern laparoscopic obesity surgery as an early intervention.

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