International Journal of Obesity (2012) 36, 1388–1395
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BARIATRIC AND METABOLIC SURGERY ORIGINAL ARTICLE

Two-year outcome of laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity: results from a Swedish Nationwide Study (AMOS)

T Olbers[1,2], E Gronowitz[1], M Werling[1], S Mårlid[1], C-E Flodmark[3], M Peltonen[4], G Göthberg[1], J Karlsson[1,5], K Ekbom[6], LV Sjöström[1], J Dahlgren[1], H Lönroth[1], P Friberg[1] and C Marcus[6]

CONTEXT: The prevalence of obesity among adolescents has increased and we lack effective treatments.
OBJECTIVE: To determine if gastric bypass is safe and effective for an unselected cohort of adolescents with morbid obesity in specialized health care.
DESIGN, SETTING AND PATIENTS: Intervention study for 81 adolescents (13–18 years) with a body mass index (BMI) range 36–69 kg m^{-2} undergoing laparoscopic gastric bypass surgery in a university hospital setting in Sweden between April 2006 and May 2009. For weight change comparisons, we identified an adult group undergoing gastric bypass surgery ($n = 81$) and an adolescent group ($n = 81$) receiving conventional care.
MAIN OUTCOME MEASUREMENTS: Two-year outcome regarding BMI in all groups, and metabolic risk factors and quality of life in the adolescent surgery group.
RESULTS: Two-year follow-up rate was 100% in both surgery groups and 73% in the adolescent comparison group. In adolescents undergoing surgery, BMI was 45.5 ± 6.1 (mean ± s.d.) at baseline and 30.2 (confidence interval 29.1–31.3) after 2 years ($P < 0.001$) corresponding to a 32% weight loss and a 76% loss of excess BMI. The 2-year weight loss was 31% in adult surgery patients, whereas 3% weight gain was seen in conventionally treated adolescents. At baseline, hyperinsulinemia (>20 mU l^{-1}) was present in 70% of the adolescent surgery patients, which was reduced to 0% at 1 year and 3% at 2 years. Other cardiovascular risk factors were also improved. Two-thirds of adolescents undergoing surgery had a history of psychopathology. Nevertheless, the treatment was generally well tolerated and, overall, quality of life increased significantly. Adverse events were seen in 33% of patients.
CONCLUSIONS: Adolescents with severe obesity demonstrated similar weight loss as adults following gastric bypass surgery yet demonstrating high prevalence of psychopathology at baseline. There were associated benefits for health and quality of life. Surgical and psychological challenges during follow-up require careful attention.

International Journal of Obesity (2012) **36,** 1388–1395; doi:10.1038/ijo.2012.160; published online 25 September 2012

Keywords: adolescent; bariatric; surgery; gastric bypass

INTRODUCTION

The health consequences for adolescents with obesity are serious. There is an increased risk of cardiovascular and endocrine disorders, metabolic syndrome, various cancers and psychosocial problems.[1–3] Taken together, quality of life and life expectancy are reduced.[4] Yet behavioral intervention constitutes the cornerstone of childhood and adolescent obesity treatment,[3] the results for adolescents are modest.[5] Among severely obese adolescents, favorable effects of non-surgical treatment seem to be very limited and clearly insufficient for long-term reduction of the health hazards associated with obesity.[6,7]

Bariatric surgery in adults results in long-term weight loss, decrease in mortality and morbidity and improvements in quality of life.[8–11] However, surgery is not generally endorsed under the age of 18 years.[12] O'Brien *et al.*[13] recently published a well-designed randomized trial between lifestyle intervention and laparoscopic gastric banding for adolescents demonstrating a favorable weight loss and improvements in cardiovascular risk factors as well as quality of life in the surgical group. Gastric bypass is, however, the most frequently used bariatric procedure worldwide and previous small case series have demonstrated feasibility in adolescents.[12]

This paper addresses the safety and efficacy of using laparoscopic Roux-en-Y gastric bypass (gastric bypass) surgery in a cohort of adolescents refractory to conventional treatment in tertiary medical centers. Weight changes over 2 years in the adolescent gastric bypass group were compared with those in an adult group undergoing gastric bypass and with those in a conventionally treated obese adolescent group. The primary endpoint was body mass index (BMI). In the adolescent surgery group, changes in metabolic risk factors and quality of life as well as adverse events were secondary endpoints.

[1]Department of Surgery, Sahlgrenska Academy at University of Gothenburg, Medicine, Clinical Physiology and Paediatrics (Queen Silvia Children's Hospital), Gothenburg, Sweden; [2]Department of Surgery, Imperial College, London, UK; [3]Childhood Obesity Unit, Skåne University Hospital, Malmö, Sweden; [4]National Institute for Health and Welfare, Helsinki, Finland; [5]Center for Health Care Sciences, Örebro University Hospital, Örebro, Sweden and [6]Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden. Correspondence: Dr T Olbers, Department for Gastrosurgical Research and Education, Sahlgrenska University Hospital, 41345 Gothenburg, Sweden.
E-mail: torsten.olbers@gmail.com
Received 27 April 2012; revised 24 August 2012; accepted 26 August 2012; published online 25 September 2012

MATERIALS AND METHODS

In this study (AMOS—adolescent morbid obesity surgery), we report baseline characteristics and 1- and 2-year outcomes for adolescent patients recruited between February 2006 and June 2009 undergoing gastric bypass surgery. In addition, we present the weight outcome over 2 years in an adult group undergoing gastric bypass surgery and in a conventionally treated matched adolescent group.

All adolescent subjects in the study had achieved treatment according to Swedish standards, before inclusion. This treatment mainly consists of individualized or family-based counseling and cognitive behavior therapy concerning diet and physical activity.[6] Low-calorie diets and drugs (metformin, orlistat or sibutramin) were prescribed if found clinically indicated by the treating pediatrician. This treatment continued in the conventional treatment group. Thus, these adolescents were not treated according to a prospective protocol.

According to the results in a pre-study, we expected to have 90% power to determine differences in BMI when using 25 patients in each group at $P<0.01$ level. However, to achieve sufficient power for assessing changes in secondary endpoints (quality of life, metabolic changes), we expected to need 70 patients in each group for 80% power at $P<0.05$ level. The regional ethics committee approved the study protocol (523–04) and the study was conducted according to the Declaration of Helsinki.

Adolescents treated with gastric bypass

All eligible adolescents in three specialist pediatric units (Stockholm, Gothenburg and Malmö) were offered assessment for gastric bypass surgery, if they had participated for at least 1 year in a comprehensive weight loss program.

Eligibility criteria

- Age 13–18 years.
- BMI $\geqslant$40 or $\geqslant$35 kg m^{-2} with comorbidity (type 2 diabetes, sleep apnea, joint pain and high blood lipids).
- Pubertal Tanner stage $>$III and passed peak height growth velocity.

Exclusion criteria

- Insufficiently treated psychiatric disorder.
- Ongoing drug abuse.
- Obesity due to syndromes or monogenic disease as clinically assessed (50% had the MC4 receptor sequenced) or brain injury.

One hundred eligible adolescents were recruited and assessed by pediatricians, psychologists and dieticians between February 2006 and April 2009. In all, 18 declined and 82 patients opted for surgery. One patient refused surgery on the planned day of the operation. Thus, 81 individuals (35% boys) underwent surgery (Supplementary Figure 1).

Adults treated with gastric bypass

Eighty-one obese adults, undergoing gastric bypass at the same institution as adolescents, were matched by gender with the obese adolescents obtaining surgery, ensuring that date of surgery coincided within ±1 month. The inclusion age was 35–45 years at surgery; all other inclusion and exclusion criteria were similar to adolescents. Data were collected from SOReg (Swedish Obesity surgery Register).

Adolescents receiving conventional treatment

We identified a matched adolescent group from the Swedish Childhood Obesity Treatment Register (BORIS)[6] at the end of the recruitment period of surgical subjects. Eighty-one adolescents (43% boys) were selected as conventional treatment comparisons using the same inclusion and exclusion criteria as for the adolescents undergoing surgery. The date of surgery for a surgical patient coincided in time with baseline weight and height registration for a control within ±1 month. In addition, controls were selected so that the mean values of the matching variables (BMI, age and gender) in the control group moved as much as possible in the direction of the mean values in the surgically treated adolescents. Our initial strategy (presented at clinicaltrials.gov) to recruit eligible adolescents not interested in surgery as controls, was not successful as most adolescents unexpectedly accepted the surgical intervention.

The conventional treatment group achieved treatment according to Swedish standards (see above).

Anthropometry

Height was measured to the closest 0.5 cm using a wall-mounted standard stadiometer in standing position. Weight was measured in light clothing to the nearest 0.1 kg on an electronic scale, which was calibrated at regular intervals. BMI (kg m^{-2}) was calculated as weight (in kilograms) by height (in meters) squared. Excess BMI was defined as the weight above BMI 25 in patients above 18 years and iso-BMI (adjusted for age and sex) above 25 in patients below 18 years.[14] We calculated the total weight loss, percentage of excess BMI loss, change in BMI and BMI s.d. score. The BMI s.d. score (*z*-score) is the number of s.d. that a patient's BMI deviates from the reference BMI for that age group in a Swedish national reference cohort.[15]

Surgery

Surgical patients were instructed to remain on a low-calorie diet (commercially available LCD 800–1200 Kcal daily) for the 3 weeks before surgery. The laparoscopic Roux-en-Y gastric bypass consisted of a small ($<$20 ml) gastric pouch and an ante-colic, ante-gastric Roux-en-Y construction with a 80 cm long Roux limb and without closure of mesenteric windows as described in detail elsewhere.[16] The gastro-jejunostomy was constructed by linear stapling and complementary hand suturing. All subjects were operated at Sahlgrenska University Hospital, Gothenburg, by either of two experienced bariatric surgeons assisted by a pediatric surgeon.

Follow-up

The adolescent surgical patients were assessed 1 month before surgery and 2, 3, 6, 12 and 24 months after surgery. First postoperative study visit was to the bariatric surgeon and following study visits were at the pediatric outpatient clinic. If required there were support of adult staff and additional visits and assessment by a bariatric surgeon. Body weight, height, blood pressure, biochemical analyses and quality of life assessment were performed preoperatively and at 12 and 24 months after surgery. Adolescents were prescribed a daily multivitamin and mineral supplement (an ordinary commercially available), vitamin B_{12} (1 mg day^{-1}) and calcium (1 g day^{-1}) + vitamin D (800 IU day^{-1}) combination tablets after surgery. Females were prescribed iron (Fe^{2+} 100 mg day^{-1}) in addition.

In the adult group, weight and height was measured and registered prospectively at inclusion and 1-year postoperatively. Two-year weight data were measured at community health-care center in most cases but were self-reported if lacking data.

In the adolescent obese controls, weight and height were measured at baseline and after 1 and 2 years and registered prospectively. Biochemistry and quality of life data will be collected at the 5-year follow-up for this group.

Laboratory examinations and blood pressure

Blood samples in adolescent surgical patients were taken in the morning, after fasting from 2200 hours the evening before. The following analyses were performed at accredited biochemical laboratories: glucose, insulin, HbA1c, triglycerides, high-density lipoproteins, low-density lipoproteins, apolipoproteins A and B, high-sensitive C-reactive protein, white blood cell (WBC) count, hemoglobin, platelets, aspartate and alanine transferases (AST, ALT), alkaline phosphatases (ALP), bilirubin, ferritin, iron (Fe), vitamin B_{12}, homocysteine, sodium, potassium, calcium, albumin and creatinine. Blood pressure was measured following 10-min rest.

Health-related quality of life

A Swedish version of Short Form-36 Health Survey (SF-36) v2 that has been validated for use in adolescents was used to measure generic health-related quality of life in the adolescent surgical patients.[17] SF-36 comprises eight general health domains and corresponding scores range from 0 to 100, with higher scores indicating better health status. In addition, summary scores for physical and mental health were calculated using norm-based scoring with a mean of 50 (greater scores representing better health status).

Adverse events

Thirty-day surgical complications data were assessed at the 2 month follow-up visit. Adverse events were thereafter continuously recorded in an e-CRF (electronic case record file system) in the adolescent surgical patients. A complementary retrospective survey of medical records was

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conducted to capture missing data before concluding results. A presentation of all adverse events on an individual basis is given in Supplementary Table 1.

Statistical analysis

Descriptive statistics are given as means with s.d. or medians with range. Changes over time are expressed with 95% confidence intervals (CI). Multilevel mixed-effect regression models were fitted to the data to assess changes over the study period. In the analyses, observations were considered nested within persons, and standard errors were therefore calculated by taking into account the repeated measurements. For comparisons between the surgically treated adolescents, surgically treated adults and the conventionally treated adolescent control group, an interaction term between treatment group and time was included in the models, and its statistical significance was evaluated.

All *P*-values are two-tailed and $P<0.05$ was considered statistically significant. Statistical analyses were carried out using the Stata statistical package 10.1 (Stata-Corp, 2007, Stata Statistical Software: Release 10.1, College Station, TX, USA; StataCorp LP).

RESULTS

Baseline characteristics

Conventionally treated adolescents had a somewhat lower BMI than surgically treated adolescents at baseline (BMI 42.0 vs 45.5, respectively), and corresponding values for BMI s.d. score were 3.9 vs 4.1. The proportion of males was 35% in both surgical groups and 43% in conventionally treated adolescents. The mean body weight at inclusion was 133 kg in the adolescent surgery group, 127 kg in adult surgery group and 124 kg in conventionally treated adolescents. Mean ages were 16.5 years for adolescents undergoing surgery, 39.7 years for the adults and 15.8 years for the conventionally treated adolescents (Table 1).

In the adolescent surgical group, 25 (31%) had neuropsychiatric diagnoses, 13 (16%) had previous self-destructive behavior and 33 (41%) had contact with pediatric psychiatric units. Poor school performance (truancy, leaving school without a diploma) was frequently reported (>50%). Only 26 adolescents (32%) had no recorded psychosocial problems.

Table 1. Baseline characteristics

	Surgery adolescents	*CCs*	*Surgery ACs*
Number			
Total	81	81	81
Male/female	28/53	35/46	28/53
Age (years)			
Total	16.5 (1.2)	15.8 (1.2)	39.7 (2.9)
Male	16.6 (1.3)	15.9 (1.2)	40.2 (3.5)
Female	16.5 (1.1)	15.7 (1.3)	39.5 (2.6)
Height (m)			
Total	1.71 (9.3)	1.71 (9.3)	1.71 (0.1)
Male	1.78 (10.4)	1.78 (7.9)	1.82 (0.1)
Female	1.67 (6.4)	1.66 (7.7)	1.66 (0.1)
Weight (kg)			
Total	133 (22)	124 (21)	127 (20)
Male	147 (23)	135 (20)	142 (17)
Female	125 (17)	115 (17)	120 (17)
BMI (kg m^{-2})			
Total	45.5 (6)	42.2 (5)	43.5 (5)
Male	46.7 (6)	43.0 (5)	43.1 (6)
Female	44.8 (6)	41.6 (5)	43.7 (5)
BMI (SDS)			
Total	4.1 (0.45)	3.9 (0.39)	ND
Male	4.4 (0.45)	4.0 (0.39)	ND
Female	4.1 (0.43)	3.9 (0.39)	ND

Abbreviations: AC, adult control; BMI, body mass index; CC, conservative control; ND, not determined; SDS, s.d. score. Data are shown as mean (s.d.).

Primary hospitalization and postoperative complications

Median surgical time was 63 min (range 38–106) in the adolescent group. Median postoperative stay was 4 days (range 2–11). There was no mortality and none required treatment in the intensive care unit. Two patients required blood transfusions because of intra-abdominal hemorrhages not requiring any surgical intervention and another was re-hospitalized for 5 days shortly after being discharged and received intravenous antibiotics because of an intra-abdominal infection where a computed tomography scan showed signs of intra-abdominal infection but no leakage. No other 30-day postoperative morbidity was recorded (Supplementary Table 1).

Follow-up rates

There was a 100% follow-up rate at 1 and 2 years for weight and height in both groups undergoing surgery. In the conventionally treated adolescent group, there was a 100% follow-up for weight after 1 year, and 73% (59 individuals) after 2 years (Supplementary Figure 1). None in the conservatively treated comparison group had bariatric surgery over the 2-year follow-up.

Weight changes

As illustrated in Figure 1, the mean BMI decreased from 45.5 to 30.2 kg m^{-2} ($P<0.001$, CI −16.6 to −14.0 for change) in the adolescent surgery group and from 43.5 to 29.7 kg m^{-2} ($P<0.001$, CI −14.9 to −12.6 for change) in the adult surgery group over 2 years after surgery ($P=0.55$ between groups). BMI did not change in conservatively treated adolescent group: 42.2 kg m^{-2} preoperatively and 42.6 kg m^{-2} 2 years postoperatively (CI −0.6 to 2.2 kg m^{-2} for change). Corresponding weight changes were −32% (CI −35 to −30%), −31% (CI −34 to −29%) and +3% (CI 0 to 7%), respectively, and 93% of adolescents achieved >50% excess BMI loss. BMI s.d. score in the adolescent surgical group decreased equally significant to when using regular BMI.

There were no significant weight change between 1 and 2 years in surgical groups and no significant differences in the weight loss between genders in the adolescent group undergoing surgery (Table 2, Figure 1, Supplementary Figure 2).

Metabolic changes

Metabolic changes were assessed only in the surgically treated adolescent group (Figure 2, Supplementary Figure 3). One patient had type 2 diabetes at inclusion but not during follow-up. None of surgically treated adolescents developed type 2 diabetes, neither were anybody treated with anti-hypertensive or lipid lowering drugs or because of sleep apnea either at baseline or during follow-up. Two-year blood samples were collected in 78 out of 81 participants (96%). Seventeen (21%) patients had elevated fasting glucose (fasting plasma glucose 5.5–7.0 mmol l^{-1}) at baseline, remaining in four of them at 2-year follow-up. Fasting insulin, however, was reduced from 31.2 (CI 27.3–35.2) mU l^{-1} at baseline to 7.6 (CI 6.6–8.7) mU l^{-1} at the 2-year examination ($P<0.001$). The proportion of subjects above the fasting insulin reference value (20 mU l^{-1}) decreased from 70% at baseline to 0% at year 1 and to 3% at year 2. HbA1C was significantly reduced at year 1 and 2. Blood lipids were ameliorated, as demonstrated in Figure 2 and Supplementary Figure 3. Fasting triglycerides above reference level (1.6 mmol l^{-1}) was found in 19% preoperatively but in only 2.5% of adolescents after 1 year and 1% after 2 years, and 33% had a low-density lipoprotein above reference value at baseline and 16% at 2-year follow-up.

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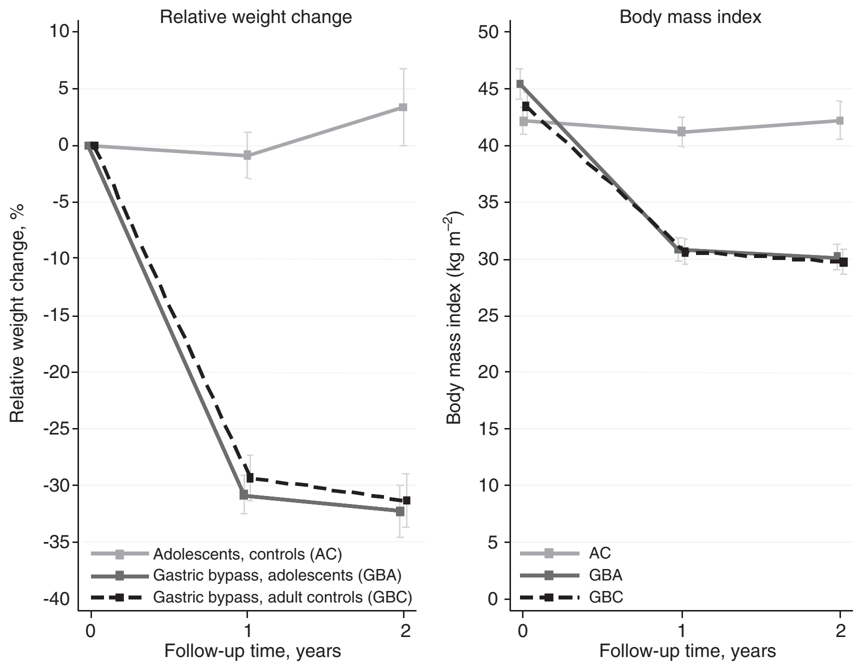

Patients, n:						
AC	81	81	59	81	81	59
GBA	81	81	81	81	81	81
GBC	81	81	81	81	81	81

Figure 1. Weight changes in adolescents and adults after gastric bypass and in an adolescent control group. Changes over 2 years in relative weight and BMI in adolescents and adults undergoing gastric bypass surgery ($n = 81 + 81$) and adolescents in conventional treatment ($n = 81$). Values are shown as mean (95% CI). Significant changes for both surgical groups ($P < 0.001$), but no difference in between surgical groups ($P = 0.55$).

Inflammatory markers decreased postoperatively and a pathological high-sensitive C-reactive protein ($>5\,mg\,l^{-1}$) was demonstrated in 59% preoperatively but only in 11% after 1 year and 7% after 2 years. Blood pressure and liver function tests (AST, ALT and ALP) also improved postoperatively (Figure 2, Table 2).

Changes in quality of life

At 1-year follow-up, significant improvements were observed in seven of the eight SF-36 health domains and in the physical component summary score (Figure 3, Supplementary Figure 4). After 2 years, significant improvements compared with baseline were evident in all four physical health domains, in the physical component summary score, and in two of the four mental health domains. Minor decreases in SF-36 scale scores between 1- and 2-year follow-up did not reach significance.

Adverse events in surgically treated adolescents

Twelve adolescents (15%) underwent additional surgical interventions. Five needed an operation for internal hernia (three behind jejuno-jenunostomy and two at Petersen's space); five underwent cholecystectomy because of symptomatic gallstones. One was laparoscopically operated with finding of adhesions and one underwent emergency laparotomy because of abdominal pain without obvious pathology. Four other visited an emergency ward because of nonspecific abdominal pain.

Six patients (7%) had periods of impaired psychiatric health. Two girls attempted suicide with medication overdoses, one (aged 15) suffered from continued bullying and the other (aged 16) had persistent depression and anxiety. An 18-year-old boy demonstrated self-destructive behavior and expressed suicidal ideation. Three girls were referred to an adult psychiatric unit because of depression and anxiety. No psychiatric adverse event occurred in patients who were mentally healthy at baseline.

In addition, five patients (5.2%, three girls and two boys) reported excessive use of addictive substances (drugs and alcohol) postoperatively. All of them had an existing but hidden addiction at inclusion. There was one unwanted pregnancy in a 16-year-old girl. No other psychosocial adverse event occurred in patients who were mentally healthy at baseline and thus we have no indications that surgery was associated with debut of psychosocial illness among adolescents without any psychological morbidity before surgery.

The serum levels of iron and vitamin B_{12} increased at a group level over the 2 years. However, there was an increase in the proportion of subjects with a subnormal level of ferritin from 12% preoperatively to 39% 2 years postoperatively. Subnormal vitamin B_{12} levels were found in 1.3% preoperatively and 13% 2 years postoperatively (Table 2). We identified poor compliance in the intake of the prescribed vitamin and mineral supplements in two-thirds of patients.

Most adolescents having undergone surgery experienced problems with excessive skin following weight loss. This aspect was, however, not addressed in this study since the assessment and possible intervention is not suggested until 2 years postoperatively.

DISCUSSION

We have demonstrated substantial weight loss (32%) over 2 years following gastric bypass surgery in adolescents with severe obesity. The weight loss was similar to what was found in an adult comparison group (31%), whereas no weight loss was seen in the adolescent group in conventional treatment. Fasting insulin was markedly reduced in the adolescent surgery group and other cardiovascular risk factors were also improved. Finally, quality of life was improved, although psychological and surgical adverse events occurred.

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Table 2. Biochemical data and BP in gastric bypass operated adolescents with severe obesity at baseline, 1 and 2-year follow-up

	Baseline	n	*1-Year post-surgery*	n	*P-value 1 year vs baseline*	*2-Year post-surgery*	n	*P-value 2 years vs baseline*	*P-value 2 years vs 1 year*
	Total		Total			Total			
Weight (kg)	132.8 (128.0–137.7)	81	91.6 (88–95)	81	$<$0.0001	89.4 (85.5–93.3)	81	$<$0.0001	NS
Height (cm)	170.8 (168.7–172.8)	81	171.7 169.7–173.8)	81	$<$0.0001	172.0 (169.9–174.1)	81	$<$0.0001	0.003
BMI	45.5 (44.1–46.8)	81	30.8 (29.8–31.8)	81	$<$0.0001	30.2 (29.1–31.2)	81	$<$0.0001	0.02
BMI SDS	4.2 (4.1–4.3)	81	2.6 (2.4–2.8)	81	$<$0.0001				
Hb (g l^{-1})	139 (137–142)	78	135 (132–138)	81	0.0003	132 (129–136)	79	$<$0.0001	NS
WBC ($\times$10*9 l^{-1})	8.2 (7.8–8.6)	77	6.5 (6.1–6.8)	81	$<$0.0001	6.5 (6.1–7.0)	78	$<$0.0001	NS
Platelets ($\times$10*9 l^{-1})	312 (297–328)	77	268 (254–283)	81	$<$0.0001	267 (252–281)	78	$<$0.0001	NS
Albumin (g l^{-1})	40.1 (39.2–40.9)	78	39.8 (39.2–40.5)	79	NS	39.1 (38.4–39.4)	78	0.02	NS
Calcium (mmol l^{-1})	2.33 (2.31–2.35)	78	2.35 (2.33–2.37)	80	0.05	2.32 (2.30–2.34)	78	NS	0.002
Na (mmol l^{-1})	141 (140–141)	78	142 (141–142)	80	0.002	141 (141–142)	78	NS	NS
K (mmol l^{-1})	4.1 (4.0–4.1)	78	3.9 (3.8–4.0)	80	$<$0.0001	3.9 (3.9–4.0)	79	NS	NS
Creatinine (umol l^{-1})	61.5 (59.4–63.6)	80	60.3 (58.4–62.2)	81	NS	60.8 (58.9–62.6)	78	NS	NS
AST (ukat l^{-1})	0.50 (0.46–0.54)	80	0.39 (0.37–0.42)	80	$<$0.0001	0.39 (0.36–0.42)	79	$<$0.0001	NS
ALT (ukat l^{-1})	0.63 (0.54–0.72)	80	0.36 (0.33–0.40)	80	$<$0.0001	0.35 (0.31–0.38)	79	$<$0.0001	NS
ALP (ukat l^{-1})	1.71 (1.57–1.85)	80	1.54 (1.41–1.67)	81	0.0005	1.42 (1.3–1.5)	68	$<$0.0001	0.001
Bilirubin (umol l^{-1})	9.6 (8.3–10.8)	75	11.5 (10.2–12.8)	80	$<$0.0001	11.1 (9.7–12.6)	78	0.0006	NS
P-glucose (mmol l^{-1})	5.1 (4.9–5.2)	80	4.9 (4.7–5.0)	74	0.03	5.0 (4.9–5.1)	77	NS	NS
P-insulin (mU l^{-1})	31.1 (27.3–35.2)	79	7.3 (6.6–8.0)	80	$<$0.0001	7.6 (6.4–8.7)	78	$<$0.0001	NS
HbA1C (%)	4.4 (4.3–4.5	80	4.2 (4.1–4.3)	80	$<$0.0001	4.2 (4.1–4.3)	77	$<$0.0001	NS
TG (mmol l^{-1})	1.3 (1.2–1.4)	80	0.9 (0.8–1.0)	80	$<$0.0001	0.8 (0.7–0.9)	78	$<$0.0001	0.02
LDL (mmol l^{-1})	2.61 (2.5–2.8)	81	1.99 (1.9–2.1)	79	$<$0.0001	1.92 (1.8–2.0)	77	$<$0.0001	NS
HDL (mmol l^{-1})	1.09 (1.0–1.1)	81	1.37 (1.3–1.4)	80	$<$0.0001	1.49 (1.4–1.6)	78	$<$0.0001	0.0008
Apo A1 (g l^{-1})	1.16 (1.1–1.2)	80	1.33 (1.3–1.4)	80	$<$0.0001	1.43 (1.4–1.5)	77	$<$0.0001	0.0003
Apo B (g l^{-1})	0.87 (0.8–0.9)	80	0.68 (0.6–0.7)	80	$<$0.0001	0.66 (0.6–0.7)	77	$<$0.0001	NS
Fe (umol l^{-1})	13.1 (11.9–14.3)	77	16.0 (14.3–17.8)	72	0.001	17.6 (15.6–19.6)	66	0.0002	NS
Ferritin (ug l^{-1})	60.4 (52.1–79.5)	64	53.7 (42.6–64.8)	78	NS	45.1 (32.7–57.6)	76	NS	0.04
B_{12} (pmol l^{-1})	315 (293–337)	73	357 (303–412)	77	NS	350 (297–403)	76	NS	NS
Homocystein (umol l^{-1})	10.5 (9.3–11.6)	74	14.2 (11.9–16.6)	79	0.005	12.3 (11.2–13.5)	77	$<$0.0001	NS
hs-CRP (mg l^{-1})	7.2 (5.9–8.6)	74	2.5 (1.3–3.7)	71	$<$0.0001	2.8 (0.4–5.2)	71		NS
Waist cc (cm)	131 (127–134)	78	102 (99–105)	80	$<$0.0001	101 (98–105)	74	$<$0.0001	0.02
BP systolic (mm Hg)	125 (122–127)	72	117 (114–119)	81	$<$0.0001	117 (114–121)	74	$<$0.0001	NS
BP diastolic (mm Hg)	77 (75–79)	77	70 (68–72)	81	$<$0.0001	70 (68–93)	74	$<$0.0001	NS

Abbreviations: ALP, alkaline phosphatase; AST and ALT, aspartate and alanine transferases; Apo A1, apolipoprotein A1; Apo B, apolipoprotein B; BMI, body mass index; BP, blood pressure; Fe, iron; HB, hemoglobin; HDL, high-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; LDL, low-density lipoprotein; NS, nonsignificant; SDS, s.d. score; TG, triglyceride; WBC, white blood cell. Data are shown as mean (95% CI).

Conventional treatments for obesity in adolescents have a generally poor outcome[6] and new treatment alternatives are needed. A recent randomized controlled trial demonstrated that laparoscopic gastric banding is superior to conventional therapy in adolescents recruited directly from the community.[13] However, other studies have been less successful with gastric banding in adolescents and have rather recommended gastric bypass.[18] The variation in outcome between studies may partly be due to differences in study populations. Adolescents with severe obesity in hospital programs have a high prevalence of psychopathology and psychosocial problems[19–21] affecting the compliance required both for conventional treatment and follow-up after gastric banding. We consciously did not exclude patients with psychiatric and psychosocial problems in this study, making our adolescent group representative with a 68% prevalence of psychosocial problems.[19–21]

The gastric bypass might be beneficial in adolescents with a risk of reduced compliance, as the weight loss is more consistent compared with after gastric banding.[11,22,23] The weight loss after gastric bypass has recently been demonstrated to be due to alterations in gastrointestinal and central neuroendocrine signaling causing reduced hunger,[24] augmented satiety,[25–27] possibly increased energy expenditure,[28] and altered taste perception and food preference.[29,30] A strong indication that physiological mechanisms determine weight loss after gastric bypass is that 93% of adolescents in our study achieved $>$50% excess weight loss despite a low number of outpatient visits, median 5 over 2 years compared with 20 visits in the O'Brien study.[13]

We found a substantial amelioration in cardiovascular risk factors (insulin, HbA1c, blood lipids and inflammation) in adolescents after gastric bypass as previously demonstrated in adults.[9,31] A major decrease in fasting insulin levels to one-fourth of preoperative level in combination with unchanged fasting glucose indicates dramatically improved insulin sensitivity. In adults, it has recently been demonstrated that high insulin is associated with increased incidence of cardiovascular events and high insulin was the only baseline variable predicting a favorable bariatric surgery effect on cardiovascular events.[11] If these results are translatable to adolescents, our findings indicate that the future incidence of cardiovascular disease may be reduced.

Quality of life parameters according to SF-36 were also low in adolescents before surgery compared with a Swedish norm for adolescents.[17,32] After surgery, we found an overall improvement despite the high preoperative prevalence of psychosocial problems, which confirms the findings in a previous study.[33]

A previous report from this study suggests an extended postoperative support to identify psychologically vulnerable subjects as no preoperative predictor could be identified.[34] Psychiatric or addictive problems (or both) occurred in 12% of patients postoperatively, which in all cases were associated with preoperatively existing conditions. We have no indications that surgery was associated with the debut of psychosocial illness among adolescents without psychological morbidity before surgery.

In adults with severe obesity, there is an increased risk for suicidal attempts[35] and this risk might be increased after bariatric surgery.[36] Our data suggest that the suicidal risk is present also among adolescents after bariatric surgery, which needs to be taken into account in the follow-up.

Fifteen percent had surgical adverse events including five operations for internal hernia and five cholecystectomies. We currently recommend closure of mesenteric defects and medical prophylaxis for gallstones..[37,38] A majority of the adolescent

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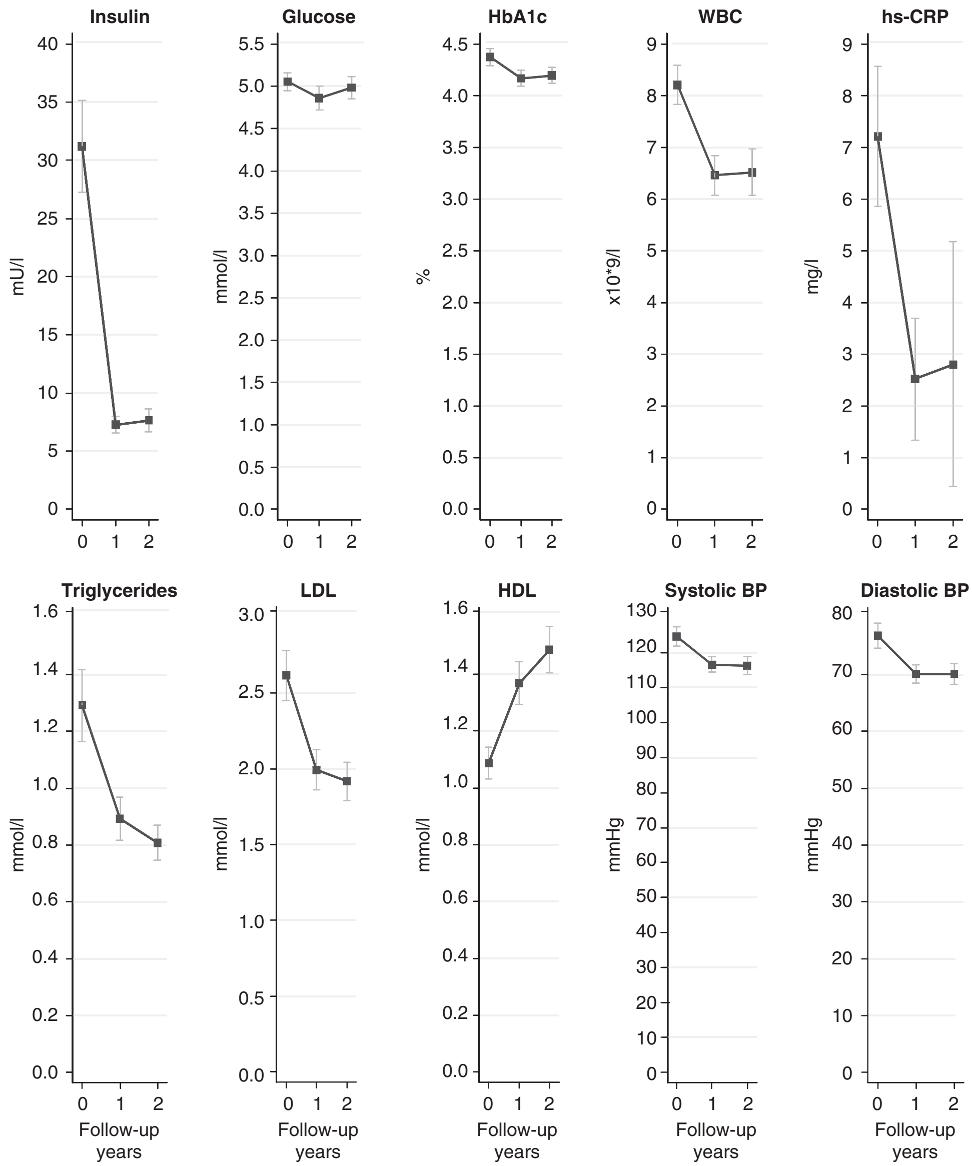

Figure 2. Biochemical and blood pressure data in adolescents after gastric bypass surgery. Biochemical data for metabolic risk factors in 81 adolescents operated with gastric bypass. Values are shown as mean (95% CI). As compared with baseline, significant improvements ($P<0.001$) were observed at 2 years with respect to insulin, HbA1c, C-reactive protein (CRP), white blood cell (WBC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and blood pressure (BP).

subjects failed to properly take their vitamin and mineral supplementation, possibly mirroring their poor psychosocial situation in combination with their age, which should be taken into account in future adolescent bariatric programs. We found a paradoxical decrease in Ferritin levels yet iron stores increased which may be a result of the decrease in general inflammatory activity.

A limitation of this study is the non-randomized setting. However, we considered it necessary to perform a broad safety and efficacy study of gastric bypass in this vulnerable group. The adult and adolescent comparison groups were identified from prospectively collected data in a national quality registers and a thorough follow-up of these groups, including an outpatient visit, is not scheduled until 5 years after inclusion. Therefore, we only have strictly collected data regarding weight and height but not biochemistry data, information about quality of life and information about psychological problems after 2 years in the comparison groups.

CONCLUSION

In summary, we have demonstrated that gastric bypass surgery results in similar weight loss in adolescents with high prevalence of psychopathology as in adults over 2 years. Furthermore, we found a substantial improvement in cardiovascular risk factors and quality of life. Nonetheless, the psychiatric adverse events appearing in this psychosocially vulnerable cohort require careful attention and might indicate limitations for the surgical strategy.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

We thank M Engström for invaluable help in setting up the study database and all the excellent staff at the pediatric obesity centers in Stockholm (C Nairn, E Forsell and G Lindmark), Gothenburg (A Laurenius, M Persson and J Curland) and Malmö

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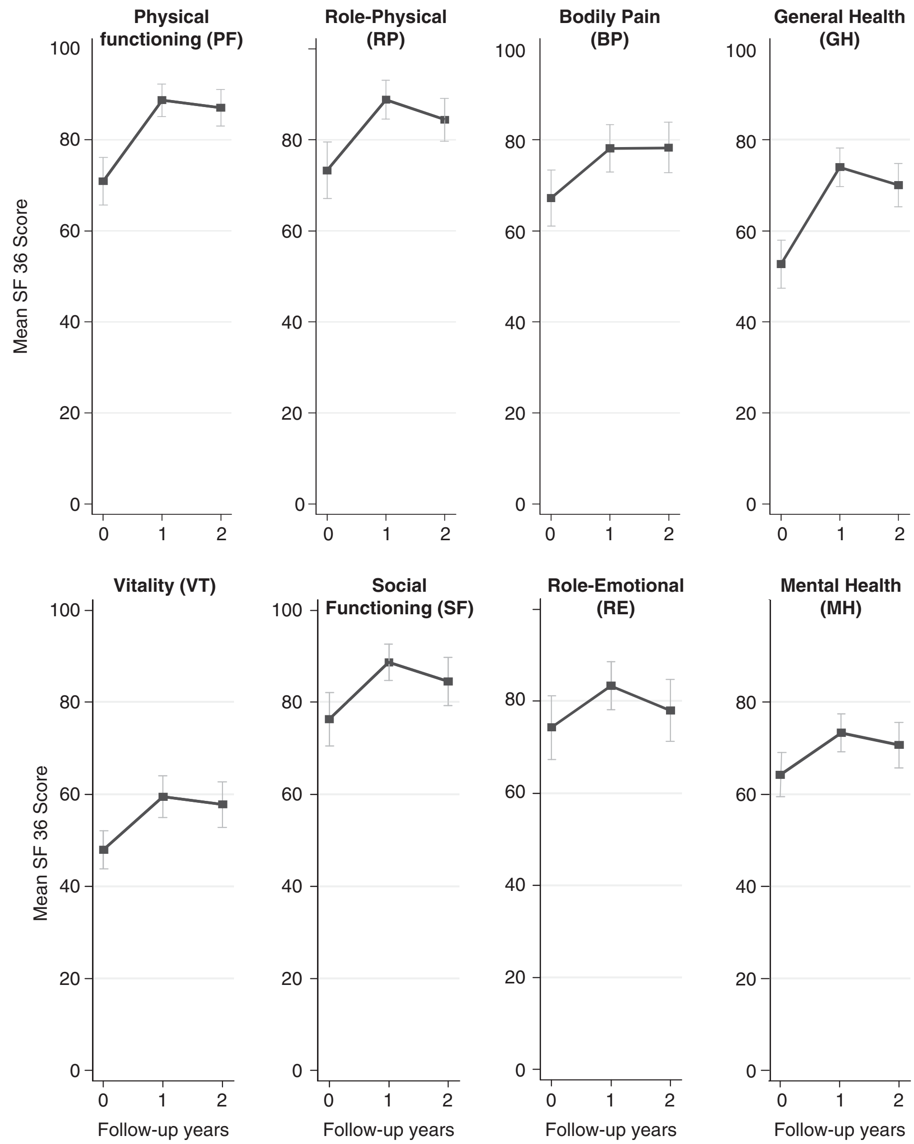

Figure 3. Quality of life data (SF-36) in adolescents after gastric bypass surgery. Observed baseline and estimated post-surgery SF-36 (Short Form-36 Health Survey) score in 81 adolescents after gastric bypass. Estimated post-surgery values are expected means from the linear mixed-effects models; a score of 0 represents worst possible health and 100 represents best possible health. Values are shown as means ±95% CI. Significant improvements ($P<0.001$) were observed at 2 years with respect to VT, PF, RP and GH, but also significant for SF ($P=0.04$) and BP ($P=0.004$). RE and MH did not show any significance after 2 years.

(K Järvholm, H Helgesson, B Bengtsson and J Derwig). The primary funding source was from Västra Götalandsregionen http://www.vgregion.se/sv/Vastra-Gotalandsregionen/startsida/ and Stockholm County Councils, Swedish Board of Health and Wellfare. Funding organizations were not involved in the design and conduct of the study or in the collection, management, analysis, and interpretation of the data. Similarly, funding organizations were not involved in the preparation, review or approval of the manuscript. Medical writers have not been used.

AUTHOR CONTRIBUTIONS

TO, MP, EG and CM had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: TO, SM, CEF and CM. Acquisition of data: TO, EG, MW, SM, CEF, GG, KE, JD, HL and CM. Analysis and interpretation of data: TO, EG, MW, SM, CEF, KE, MP, JK, LVS, JD, PF and CM. Drafting of the manuscript: TO, EG and CM. Critical revision of the manuscript for important intellectual content: TO, EG, SM, CEF, MP, GG, JK, LVS, JD, PF and CM. Statistical analysis: MP and EG. Obtained funding: TO and CM. Study supervision: TO, SM, CEF and CM.

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Supplementary Information accompanies the paper on International Journal of Obesity website (http://www.nature.com/ijo)

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