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Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity: a prospective five-year Swedish nationwide study (AMOS)

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TO, CM and EG were involved in study conception, design, data collection and analysis, and writing the manuscript. AB, GB and MN were involved in study design, data collection and analysis, and writing the manuscript. CEF, JD, KE, PF, GG, KJ, JK and SM were involved in study design, data collection and writing the manuscript. MP was involved in study design, data analysis and writing the manuscript. All authors had full access to all data and approved the final manuscript.

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Abstract

Background—Severe obesity in adolescence is associated with reduced life expectancy and impaired quality of life. Long-term benefits of conservative treatments in adolescents are limited, while short-term outcomes of adolescent bariatric surgery are promising. This study aimed to report 5-year outcomes following Roux-en-Y gastric bypass (RYGB) in adolescents, compared with conservatively treated adolescents and adults undergoing RYGB.

Methods—A nationwide prospective non-randomised controlled study of adolescents (13–18 years) with severe obesity undergoing RYGB, a matched adolescent control group undergoing conservative treatment, and an adult comparison group undergoing RYGB. The primary outcome measure was change in weight over 5 years. Multilevel mixed-effect regression models were used to assess longitudinal changes. Healthcare usage was analysed with linear regression together with nonparametric bootstrapping.

Findings—Eighty-one adolescents with baseline age 16·5 years (SD 1·2), weight 132·8 kg (SD 22·1) and body mass index (BMI) 45·5 kg/m^2 (SD 6·1) underwent RYGB. Five-year weight change was −36·8 kg (95% CI −40·9 to −32·8) resulting in a BMI reduction of 13·1 kg/m^2, although weight loss <10% occurred in 11%.

Comorbidities and cardiovascular risk factors resolved in 74–100%: type 2 diabetes (3/3), disturbed glucose homeostasis (18/21), dyslipidaemia (43/52), elevated blood pressure (11/12), inflammation (hs-CRP ≥ 2 mg/L; 45/61) and elevated liver enzymes (19/19), each comparing favourably with adolescent controls at 5 years.

Functional (SF-36) and obesity-specific (OP-14) quality of life improved in the adolescent RYGB group (mean difference 4·2, p=0·006 and −9·9 p=0·009). Twenty RYGB participants (25%) underwent additional abdominal surgery for complications of surgery or rapid weight loss, 72% demonstrated some nutritional deficiency, and healthcare consumption increased. Mean BMI increased in control adolescents (3·3 kg/m^{2,} 95% CI 1·9 to 4·8), while BMI change in adults was similar to surgical adolescents (mean difference 0·8 kg/m^2, 95% CI −1·1 to 2·8). Twenty adolescent controls (25%) underwent bariatric surgery within 5 years.

Interpretation—Adolescents with severe obesity undergoing RYGB experienced substantial weight loss over 5 years, alongside improvements in comorbidities, risk factors and quality of life. Surgical intervention was, however, associated with additional surgical interventions and nutritional deficiencies. Non-surgical treatment was associated with weight gain and 25% underwent bariatric surgery within 5 years.

Keywords

Adolescent; bariatric surgery; gastric bypass; obesity; surgery; long-term effects

Introduction

Severe obesity in adolescence is a life-threatening and life-shortening disease,[1,2] leading to a multitude of other diseases.[3,4] As the mean age of obesity onset has decreased,[5] the onset of related diseases, most notably type 2 diabetes (T2DM), has shifted increasingly toward childhood.[6] T2DM is markedly more aggressive when occurring in childhood,[6] and obesity increases cardiovascular risk factors in childhood,[7] leading to a poor prognosis in this group,[8,9] with few effective therapeutic options available.[10]

The prevalence of adolescent obesity has now reached between 5% and 10% among developed countries.[5,11,12] Non-surgical programmes remain the cornerstone of treatment of adolescents with severe obesity, although their effect is limited and insufficient for long-term reduction of obesity-related health hazards.[13] However, surgery is increasingly being recommended[14] and performed,[15] and robust outcomes have been reported up to three years after surgery.[16–18]

This study reports outcomes over 5 years in adolescents following Roux-en-Y gastric bypass (RYGB) or conservative treatment in a Swedish nationwide prospective non-randomised controlled study, with an additional matched adult comparison group undergoing RYGB.

Materials and methods

Study design

The Adolescent Morbid Obesity Surgery (AMOS) study is a Swedish nationwide prospective, non-randomised controlled study.[17] The study was conducted according to the Declaration of Helsinki with the approval of the Gothenburg regional ethics committee (523–04).

Participants

1. Adolescents treated with Roux-en-Y gastric bypass (RYGB)—All eligible adolescents presenting with severe obesity to three specialised paediatric obesity treatment units were offered assessment for surgery upon fulfilling inclusion criteria. This represented 100 patients, of whom 19 declined surgery and the remaining 81 adolescents ultimately underwent RYGB. Eligibility criteria were: age 13–18 years, BMI ≥ 40, or ≥35 kg/m^2 with comorbidity (e.g. T2DM, dyslipidaemia, metabolic syndrome), pubertal Tanner stage >III, height growth velocity beyond peak, and at least 1 year in a formal, conventional weight loss programme. Major exclusion criteria included severe psychiatric disorder, ongoing drug abuse, obesity secondary to brain injury, and syndromic or monogenic obesity (the melanocortin 4 receptor was sequenced in >50% of patients based upon clinical suspicion). Recruitment occurred between 2006 and 2009 (Fig. S1).[17]

2. Adolescents receiving conventional treatment—A matched conservatively treated adolescent control group was identified from the Swedish Childhood Obesity Treatment Register (BORIS[13]), ensuring the date of surgery was within 1 month of baseline weight for the corresponding control patient. Sequential matching of individuals ensured that the mean values of matching variables (baseline BMI, age and sex) in the control group moved closer to the mean values within the surgical group as much as was possible with each additional control patient. This registry did not include detailed formal data regarding individuals' compliance with conventional treatment.

3. Adults treated with gastric bypass—Adults aged 35–45 years with severe obesity (adult group) undergoing RYGB were matched by BMI and sex to adolescents undergoing surgery, and the same inclusion and exclusion criteria as adolescents were used.[17]

Treatments

The laparoscopic RYGB incorporated an ante-colic, ante-gastric Roux-en-Y construction with a linearly stapled gastro-jejunostomy,[19] without closure of mesenteric windows. All adolescent and adult operations were performed at Sahlgrenska University Hospital, Gothenburg, by either of two experienced adult bariatric surgeons, assisted by a paediatric surgeon. Surgical treatment of adults was delivered by the same team in an identical setting in order to maximise comparability. The control group underwent individualised treatment according to Swedish standards.[17] Within the pragmatic study design, conventional treatment was non-standardised, but was delivered as an individualised treatment by the multidisciplinary team (MDT) and focused on behaviour change.[13,20,21]

Clinical measurements

The primary outcome was change in weight across 5 years. Secondary outcomes included detailed anthropometry, biochemistry, quality of life evaluation and clinical outcomes.[17]

The term disturbed glucose homeostasis was adopted in response to incomplete data regarding fasting plasma glucose, and was defined by adding a fasting capillary glucose criterion, i.e. ≥6·1 mmol/L but <7·0 mmol/L (≥100 but <110 mg/dL), to the American Diabetes Association (ADA) definition of impaired fasting glucose, or prediabetes,[22] i.e. the absence of medication use for DM with fasting plasma glucose ≥5·5 mmol/L but <7 mmol/L (≥100 mg/dL but <126 mg/dL), or HbA1c of ≥39 mmol/mol (≥5·7%) but <45 mmol/mol (<6·5%). T2DM and its remission were also diagnosed according to ADA definitions, remission determined using the criteria FBG <7·0 mmol/L (<126 mg/dL), HbA1C <45 mmol/mol (<6·5%), fasting capillary glucose <6·1 mmol/L (<110 mg/dL) in the absence of diabetes medication.[22] All other definitions and remission criteria are provided in the web additional material.

Follow-up

Adolescent surgical patients were assessed before surgery and postoperatively at 2 and 6 months, 1, 2 and 5 years. Body weight, height, blood pressure, biochemical analyses and quality of life assessment were performed preoperatively and at 1, 2 and 5 years after surgery. Information regarding use of drugs or alcohol was sought from participants and caregivers at recruitment. Surgical adolescents were prescribed a daily multivitamin and mineral supplement (including 200 micrograms of folic acid), as well as additional vitamin B_{12} (cobalamin 1 mg /day), and calcium carbonate/ vitamin D (1 g/ 800 IU /day) tablets. Females also received iron (Fe^{2+} 100 mg /day) supplementation.

In the adolescent control group, weight and height were measured and registered at baseline and after 1, 2 and 5 years. At 5 years the control group was invited to a study visit for biochemistry and quality of life data collection.

Between years 2 and 5, adolescents were predominantly followed up in the community. In accordance with Swedish convention, systematic medical treatment for cardiovascular risk factors in youth, such as dyslipidaemia or hypertension, was not common practice.

In the adult group, weight and height were measured and registered prospectively at inclusion and 1 year postoperatively. Two- and 5-year weight data were drawn from community healthcare centre measurements, where available, and self-reported measurements otherwise.

Blood sampling and handling have been described in detail previously.[17]

Health-related quality of life

A Swedish version of Short Form-36 Health Survey v2 (SF-36), validated for use in adolescents, was used to measure health-related quality of life.[23] The Obesity-related Problems scale (OP-14) was used to assess psychosocial problems related to weight and body shape.[24]

Adverse events

Thirty-day surgical complications data in the surgical group were assessed at the 2-month follow-up visit and thereafter prospectively recorded in the electronic case record file. A complementary retrospective survey of medical records was conducted to capture missing data up to 5-year follow-up. In addition, data on inpatient care (admissions and hospital days) and hospital-based outpatient care visits were retrieved from the nationwide National Patient Register, and prescription drug costs from the Prescribed Drug Register.

Statistical analysis

Descriptive statistics are given as means with standard deviations (SD). Multilevel mixed-effect regression models were fitted to the data to assess longitudinal changes. In the analyses, observations were considered nested within persons, and standard errors were calculated by taking into account the repeated measurements. Changes over time are expressed with 95% confidence intervals (CI). The underlying assumptions for the mixed-models were evaluated through analyses of the residuals.

Among control crossovers the last observation was carried forward for anthropometric data and crossovers were excluded from analysis for all other variables. Sex- and age-adjusted mean differences for 5-year accumulated hospital days, visits for outpatient care, and prescription drug costs were estimated using linear regression with 95% CIs generated by nonparametric bootstrapping not requiring additional assumptions.

All p-values are two-tailed and $p<0{\cdot}05$ was considered statistically significant. Statistical analyses were carried out using the Stata statistical package 12·1 (Stata-Corp. 2011, Stata Statistical Software: Release 12, College Station, TX, USA; StataCorp LP).

Role of the funding source

Funders of the study did not contribute to the study design, the collection, analysis or interpretation of data, or manuscript writing.

Results

Baseline characteristics

Baseline details are given in Table 1 and Table 2. At inclusion, participants in the surgical group were older and had significantly higher BMI than the control group. The proportion of males was 44% in the control group and 35% in both surgical groups (non-significant). Mean age in the adult group was 39·7 years.

Psychosocial impairment, such as depressive or anxiety disorder, was common in the surgical group and a neuropsychiatric diagnosis was present in 31% of subjects (specific diagnoses unavailable). Sixteen percent had previously demonstrated self-destructive behaviour. Forty-one percent had previously been treated in a paediatric psychiatry outpatient department.

Follow-up rates

The follow-up rate was 100% in the surgical group, 90% (72/80) in the control group and 88% (71/81) in the adult group at 5 years. The follow up rate of our cohorts in national health care registries was 100%.

Weight outcomes

Anthropometric changes are given in Table 1 and Table 2. Mean BMI change across 5 years was −13·1 kg/m^2 (95% CI −14·5 to −11·8) in the surgical group, +3·3 kg/m^2 (95% CI +1·1 to +4·8) in the control group, and −12·3 kg/m^2 (95% CI −13·7 to −10·9) in the adult group. The proportion of participants reaching a BMI <35 kg/m^{2}was 72% (surgical), 7% (control), and 76% (adult) respectively. Thirty-seven percent of surgical group patients no longer had obesity (BMI<30), 3% in the control group, and 40% in the adult group. The majority of adolescent and adult surgical group patients achieved ≥20% total body weight loss (69% and 85% respectively), while a majority (69%) of control patients gained weight (Fig. 1b). Suboptimal weight loss was more common among adolescents than adults (p=0·035, Fig. 1b). Mean weight-regain between a nadir, observed at 2 years, and follow-up at 5 years, was similar in the operated adolescents and adults (Fig. 1a).

Twenty patients (25%) in the control group underwent bariatric surgery between follow-up years 2 and 5, having reached adult eligibility. This group had a median weight gain of 19·6 kg (range −1·1 to 53·5) from baseline until undergoing surgery, compared to a 7·3 kg (range −26·8 to 60·4) increase in control adolescents not undergoing surgery over 5 years.

Cardiometabolic risk factors

Longitudinal metabolic changes are reported for the surgical group alongside 5-year cross-sectional values for control participants in Table 2 and Table S1 (web additional material).

Glucose homeostasis

All measures of glucose homeostasis improved across 5 years (Table 2). At baseline, three patients (4%) had TD2M, all of whom were in remission 5 years after surgery. A disturbed glucose homeostasis was observed at baseline in 22 individuals (27%), which normalised in

18 patients (86%), although two new cases occurred after 5 years, resulting in a total of six cases (8%) at 5 years after surgery (Table 3). Fasting plasma insulin levels decreased markedly from 216·7 to 65·0 pmol/L (Table 2). Meanwhile, in the control group, the prevalence of disturbed glucose homeostasis was 16% at 5 years, and one new case of T2DM was observed (Table 3).

Lipids

There were 56 cases (69%) of dyslipidaemia at baseline, decreasing to 11/76 (15%) at 5 years. Notably, all cases of elevated low-density lipoprotein (LDL) or triglycerides resolved across 5 years (Table 3). The 5-year prevalence of dyslipidaemia in the control group was 73% (Table 3).

Blood pressure

Blood pressure was elevated in 12/78 (15%) participants at baseline and normalised in all 12 at 5 years, although two incident cases led to a prevalence of 3% (Table 3). The 5-year prevalence in the control group was 10% (Table 3).

Inflammation

Elevated high sensitivity C-reactive protein (hsCRP; ≥2 mg/L) was present in 87% (65/75) participants at baseline, reducing to 25% (19/77) across 5 years. In the control group hsCRP was elevated in 82% (32/39) at 5 years (Table 3).

Liver function

Elevated alanine transaminase levels were present in 25/81 (31%) surgical patients at baseline, normalising in 92% of cases (23/25) at 5-year follow-up, although there were two incident cases (Table 3). Elevated aspartamine transaminase levels, observed in 9/80 (11%), normalised in all cases across 5 years (Table 3). Alkaline phosphatase is included in Table S1 and Table S2 (web additional material).

Vitamins, minerals and general nutritional markers

At 5 years, 63% (46/73) in the surgical group and 57% in the control group (20/35) had vitamin D (25-OH D) insufficiency (<50 nmol/l; p=0.674; Table S2).

Low ferritin and/or iron levels, present in 24% (18/76) of the surgery participants at baseline, increased to 66% (51/77), compared with 29% (12/42) in the control group at 5 years (Table S2). One of 74 surgical participants (1%) had a low vitamin B_{12} level at baseline, increasing to 16/73 individuals (22%) at 5 years, when the prevalence was 6% (2/31) in the control group (Table S2).

The prevalence of anaemia (haemoglobin in females <120 g/dL; males <130 g/dL) in the surgical group rose from 10% (8/78) to 32% (25/77) across 5 years, while in the control group it was 7% (3/42) at 5 years (Table 3).

Quality of life

At 5-year follow-up, significant improvements were observed among adolescent surgical patients in the physical component summary score (Table S3) and in 3 of the 8 SF-36 health domains (Fig. 2, Table S3): physical functioning (mean change 13·5, 95% CI 8·1 to 19·0), physical role functioning (mean change 11·2, 95% CI 4·0 to 18·3) and general health perceptions (mean change 12·4, 95% CI 6·5 to 18·3), all of which are within the physical domain (Fig. 2). Physical role functioning was also significantly better among surgical group patients than controls (mean difference 13·5, 95% CI 2·2 to 24·8; Table S3). Weight-related psychosocial problems improved significantly across follow-up (mean difference −13·0, 95% CI −19·6 to −6·4).

Adverse events

Across 5 years, 20 patients (25%) in the surgical group underwent 21 additional abdominal surgical interventions, excluding plastic surgery (Table 4). Eleven procedures were for acute intestinal obstruction and nine for symptomatic gallstones. No deaths occurred across 5 years of follow-up. Some patients and their caregivers withheld information about substance misuse, even before surgery. We could not obtain valid data regarding adverse events and reoperation rates in the adult comparison group.

Healthcare use and medication

Over 5 years of follow-up and including the index hospitalisation, the surgical group accumulated a mean 16·1 hospital days, compared to 2·8 in the control group (mean difference 13·0, 95% CI 7·4 to 18·6). In-hospital days related to admissions for surgical procedures, including the index surgery, accounted for 6·5 days in the surgery group compared to 1·6 days in the control group (mean difference 5·0, 95% CI 2·7 to 7·2).

The number of outpatient visits was also higher in the surgical than the control group (14·6 vs. 10·0; mean difference 4·9, 95% CI 1·3 to 8·4).

Total prescription drug costs over 5 years were similar in the surgical and control groups ($2317 vs. $2701; mean difference −$611, 95% CI −3252 to 2030).

Discussion

Most adolescents undergoing RYGB for severe obesity in this study experienced substantial weight loss, metabolic improvement, reduction of the chronic inflammatory state and enhancement of quality of life, which remained 5 years after surgery. Concurrently, a control group undergoing conventional treatment experienced progressive weight gain.

RYGB resulted in a mean 29% weight loss after 5 years, which is comparable to the 28% reduction after three years reported in the Teen-LABS study.[16] Rapid weight reduction during the first year was followed by modest weight regain between 2 and 5 years. The matched adult group, operated at the same centre, experienced a similar mean weight reduction. However, a greater variability in long-term weight outcome in adolescents, compared with adults, may indicate greater phenotypical heterogeneity and/or a greater need for postoperative support to optimise outcomes.

We and others have previously reported that metabolic risk factors and comorbid conditions improve markedly in adolescents 2 to 3 years after surgery.[16–18] In this study we confirm that these positive trends remain after 5 years. We observed an amelioration of disturbed glucose homeostasis, dyslipidaemia and high blood pressure. We also found a substantial reduction in hsCRP following surgery, suggesting improvement of the chronic inflammatory state, which has been demonstrated to be a contributor to cardiovascular comorbidity development.[25,26] At 5 years, metabolic risk factors, such as dyslipidaemia and elevated liver enzymes, were more prevalent in the control group than the surgical group, although direct comparison between the two adolescent groups was influenced by the crossover of participants to undergo RYGB during follow-up. Since individuals with the most severe weight gain underwent surgery during follow-up, the control group became progressively "healthier" across the follow-up period.

Gastric bypass surgery is associated with an inherent risk of developing vitamin and mineral deficiencies related to impairment of absorption and decreased food intake. Therefore, nutritional supplements were prescribed, according to Scandinavian clinical standards at that time. At 5 years after surgery we found a concerning prevalence of iron deficiency, associated low haemoglobin levels, and also vitamin D insufficiency. Poor compliance with supplementation may have contributed to this, as previously described. [17] This is an important area for improvement and recent guidance suggests adopting more aggressive supplementation, such as higher doses of vitamin D, as well as more effective compounds, such as calcium citrate rather than calcium carbonate. Regular access to long-term follow-up between 2 and 5 years may have ameliorated nutritional deficiencies.

Psychosocial impairment is highly prevalent in adolescents with severe obesity, [27] as was observed at baseline in this study. [17,28] We demonstrated improvement in obesity-related psychosocial problems in the surgical group over 5 years, as well as in generic self-reported quality of life, most notably in participants' perceived general health and physical function. Improvements did not, however, occur across all aspects of quality of life, which should be communicated to patients and their families preoperatively to manage expectations. Specific attention must also be paid to identifying and helping individuals at risk of self-harm and suicide in this vulnerable group.

The accumulated in-hospital stay across 5 years was longer in the surgical group than the control group, which is in line with expectations given the primary procedure and incidence of complications and remedial interventions in the surgical group.[29] Thus, the obesity-related comorbid diseases observed in control adolescents, did not lead to a greater need for in-hospital treatments within 5 years of follow-up. Despite including routine prescribed nutritional supplementation, the observed costs of medication were no greater in the surgical group than the control group.

The rate of additional procedures in the surgical group was higher than that reported within the Teen-LABS study,[16] primarily due to a high rate of intra-abdominal herniation associated with non-closure of mesenteric defects. [30] Also contributing was a higher rate of cholecystectomy for gallstones in our study; a consequence of significant rapid weight loss.[31] Rates of small bowel obstruction and cholecystectomy were, however, similar in

Swedish adults undergoing the RYGB.[30,32] Recent advances in practice have enabled reduction in the incidence of both internal herniation and gallstone formation by performing primary closure of mesenteric defects[30] and administration of ursodeoxycholic acid prophylaxis,[32] suggesting that the rate of additional surgery can be reduced by more than 50%. [30,32]

The overall risk-benefit equation must, however, also take into account both the existing and imminent health implications in young persons with severe obesity and the failure of other therapies to achieve sustainable improvements.[10,13] Although a small proportion of control adolescents succeeded in reaching normal weight across 5 years (3%), not only did the vast majority (90%) fail to achieve reversal of their obesity, but most (69%) actually gained weight. Delaying surgery thus represents an avoidable prolongation of exposure to cardiometabolic risk factors, with risk of development or progression of comorbid diseases.[7]

Strengths of this study include respectable rates of retention throughout follow-up, particularly considering the nature of an adolescent population and a 5-year follow-up period. Surgical procedures in adolescents and adults were carried out by surgeons in a single centre, using a standardised and well-recognised technique,[19] refined over thousands of procedures in adults. The adult group experienced an almost identical treatment pathway, minimising bias related to the treatment. The Swedish healthcare registries guarantee an accurate quantification of postoperative healthcare and medication usage. Limitations include a non-randomised setting and a pragmatic, non-standardised conservative treatment. However, to the best of our knowledge, there is only one long-term study of a specific conservative treatment of obesity including adolescents, which achieved only modest weight loss and lost almost 40% to follow-up across 5 years.[33] A randomised controlled trial would have reduced the potential for selection bias, however, in the absence of safety and efficacy data, we considered this design challenging. Many of the adult group weight data points were self-reported, although evidence in an adult bariatric population shows that this leads to under-reporting of weight by just 0.8 to 0.9 kg,[34] allaying our concerns. There was also some attrition in our patient number regarding laboratory and quality of life measurements. A 25% crossover to surgery in the control group during follow-up limited the comparability of the adolescent groups. Due to the limited size of the study population, and therefore the low number of adverse events, adjustment was performed for age and sex alone. RYGB was the only surgical procedure performed as sleeve gastrectomy was novel at the time, although it has been used in later adolescent series.[16,35] Finally, although this is a nationwide study, caution should be exercised in generalisation to other populations and regions.

Conclusion

RYGB results in substantial weight loss, frequent resolution of cardiometabolic comorbidity, and improvement in quality of life into the long-term in adolescents suffering from severe obesity. In contrast, non-surgical treatment led to further weight gain and one in four control adolescents underwent surgery during 5-year follow up. Surgical intervention was, however, associated with a high rate of additional surgical intervention and nutritional deficiencies.

The literature base now appears sufficiently mature to consider formal integration of bariatric surgery into treatment pathways for adolescents with severe obesity. However, we consider it crucial that adolescent bariatric surgery is performed within appropriate specialist multidisciplinary programmes, designed specifically to accommodate adolescent patients and provide long-term follow-up and support.

Future challenges include refining indications and contraindications, identifying ideal target age groups, and optimisation of postoperative support. We must also closely monitor for potential long-term adverse effects of surgery, across decades rather than years.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Research in context

Evidence before this study

Before 2006 there was a large and growing body of evidence relating to bariatric surgery in adults, particularly using the Roux-en-Y gastric bypass (RYGB), but only limited experience from adolescents undergoing bariatric surgery.

We searched PubMed from 14 February, 1956 to 13 February, 2006, for “adolescent” OR “child*” AND “gastric bypass” AND “obesity”, with no restrictions on language. Of 246 items returned, we identified 6 relevant retrospective case series, including between 4 and 39 genetically normal patients undergoing RYGB, and dating as far back as 1975.

With increasing awareness of the dramatic health risks associated with severe obesity in the adolescent population, and limited success among non-surgical treatments, positive outcomes in adults prompted consideration of bariatric surgery in adolescents on a case-by-case basis in extreme circumstances. However, there was a paucity of prospective and systematic assessments of the risks and benefits in adolescents.

Within the limited existing case series, a mean BMI reduction of approximately 20 kg/m^2 was reported at least 1 year after RYGB, but there were fewer than 45 patients with follow-up to 5 years or longer. Several adolescents demonstrated improvement in obesity-related metabolic axes, such as glucose homeostasis, lipids and blood pressure following surgery.

However, while these small series were certainly promising, inherent limitations rendered their results of limited reliability and generalisability. Most studies included a small number of participants and a retrospective design, many employing suboptimal methods of follow-up, without requiring clinic attendance, yet minor to moderate complications were relatively common.

Added value of this study

The added value of this prospective study predominantly lies in three areas. Firstly this study advances knowledge and understanding of the outcomes of RYGB among adolescents with severe obesity into the long-term, where previous prospective studies have reported outcomes up to 3 years after surgery thus far. Secondly, to the best of our knowledge, the present study is the first to concurrently examine a contemporary matched adolescent control group undergoing conventional treatment, and indeed a contemporary matched adult group undergoing RYGB, embedding the observed results within the context of the existing understanding of adult outcomes. Thirdly this study adds data from several national registries, expanding the outcomes reported in the literature to include healthcare consumption. We conclude, however, that there is a need to develop targeted strategies to reduce weight regain and avoid nutritional deficiencies in operated adolescents, and also to reduce the need for additional surgery.

Implications of all the available evidence

These long-term data extend knowledge beyond existing accumulated 2- and 3-year follow-up data from the US, Europe, Saudi Arabia and Australia, which have consistently supported the use of bariatric surgery in adolescents with severe obesity. Studies have shown that RYGB, sleeve gastrectomy and adjustable gastric banding are safe and effective in achieving and maintaining weight loss and significant metabolic health gains, often inducing remission of type 2 diabetes or prediabetes, dyslipidaemia and hypertension. The current evidence base, however, also highlights the challenges presented by performing bariatric surgery in adolescents.

We consider the literature base now sufficiently mature to consider formal integration of bariatric surgery into treatment pathways for adolescents with severe obesity. However, assessment of adolescents for surgery should be embedded within formal programmes incorporating all other available obesity treatments, led by a multidisciplinary team capable of conducting physical as well as psychosocial assessments of the individual patient. Provision must also be made for long-term follow-up and management, with concern for surgical and nutritional adverse events, avoidance of weight regain, and also for continuous psychological support when needed, knowing that this is a vulnerable patient group.

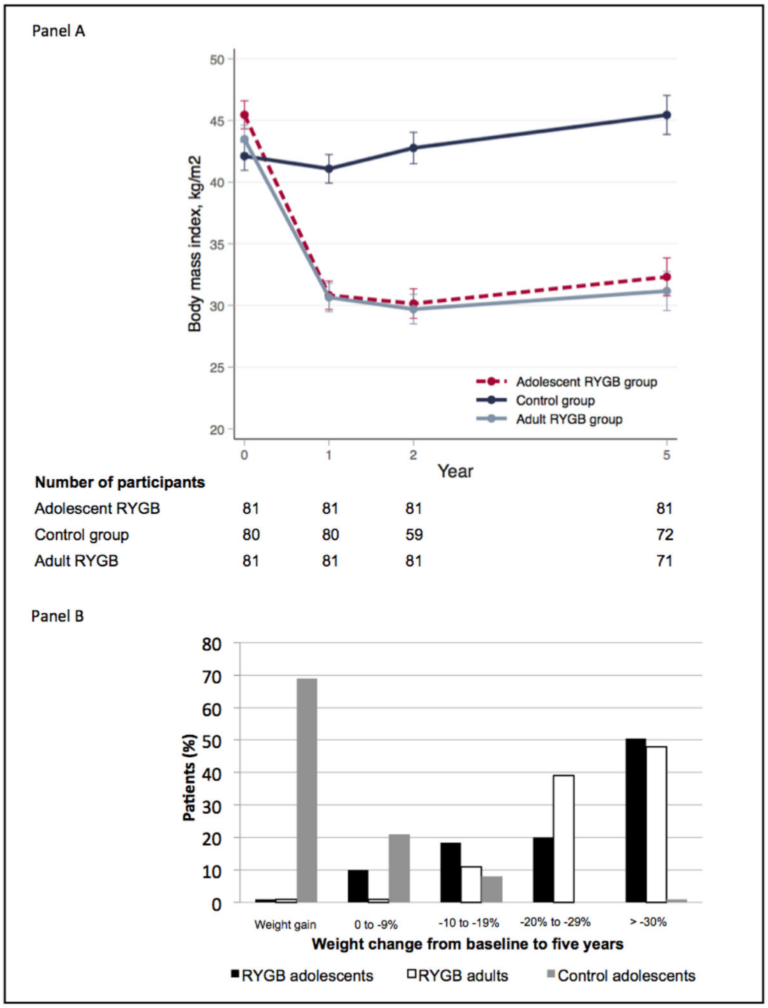

Figure 1. Body mass index (panel A) and weight (panel B) change from baseline to 5 years

Control adolescent data are presented using the last observation before surgery carried forward for patients who underwent surgery within the follow-up period.

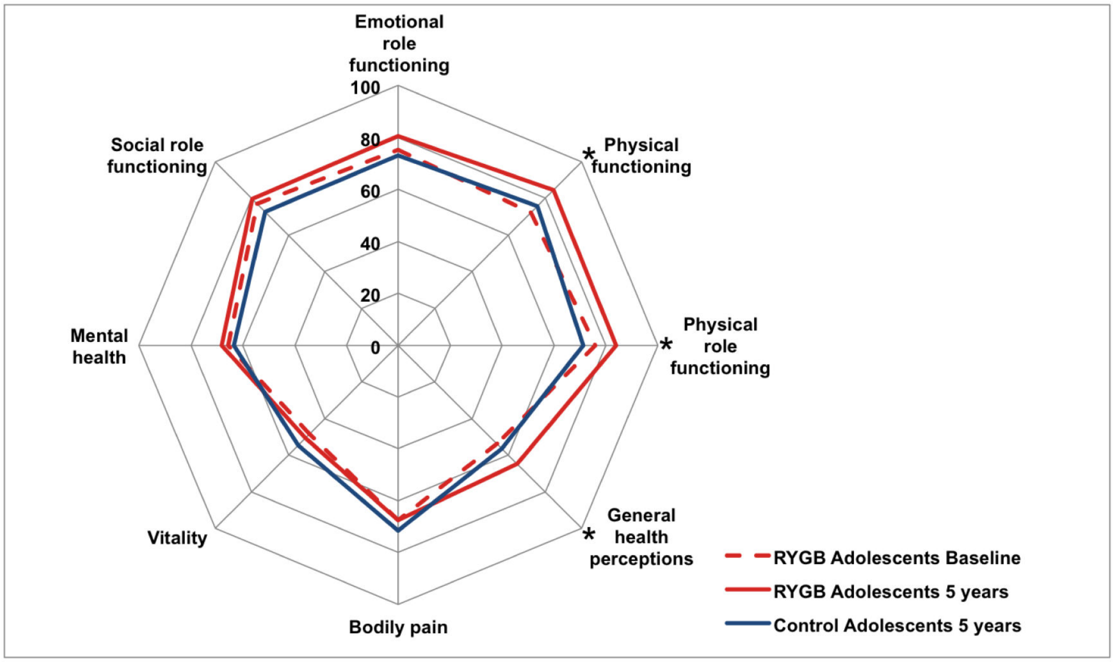

Figure 2. Polar chart showing quality of life outcomes

Data from SF-36 (short-form 36 questionnaire) scores. Asterisks indicate significant improvement between baseline and 5 years among RYGB adolescents.

Table 1

Baseline and 5-year characteristics.

	RYGB Adolescents		Control Adolescents		Gastric Bypass Adults	
	Baseline	5 years	Baseline	5 years	Baseline	5 years
Number						
Total	81	81	80	72	81	71
Male	28	28	35	30	28	23
Female	53	53	45	42	53	48
Age (years)						
Total	16·5 (1·2)	21·9 (1·2)	15·8 (1·2)	20·9 (1·3)	39·7 (2·9)	44·7 (2·9)
Male	16·6 (1·3)	22·0 (1·4)	15·9 (1·2)	21·0 (1·2)	40·2 (3·5)	45·2 (3·5)
Female	16·5 (1·1)	21·9 (1·1)	15·7 (1·3)	20·8 (1·3)	39·5 (2·6)	44·5 (2·6)
Height (cm)						
Total	171 (9)	172 (9)	171 (9)	173 (10)	171 (0)	171 (0)
Male	178 (10)	180 (9)	178 (8)	180 (8)	182 (0)	182 (0)
Female	167 (6)	168 (6)	166 (8)	167 (8)	166 (0)	166 (0)
Weight (kg)						
Total	133 (22)	96 (22)	124 (21)	124 (32)	127 (20)	90 (18)
Male	147 (23)	109 (26)	135 (20)	132 (27)	142 (17)	102 (17)
Female	125 (17)	89 (17)	115 (17)	118 (34)	120 (17)	85 (16)
BMI (kg/m^2)						
Total	45·5 (6)	32·3 (6)	42·2 (5)	41·7 (10)	43·5 (5)	31·0 (6)
Male	46·7 (6)	33·3 (7)	43·0 (5)	40·8 (8)	43·1 (6)	31·1 (6)
Female	44·8 (6)	31·8 (6)	41·6 (5)	42·3 (12)	43·7 (5)	31·0 (6)

RYGB, Roux-en-Y gastric bypass (RYGB); BMI, body mass index. Data are presented as mean (standard deviation).

Table 2

Anthropometric, biochemical and blood pressure data at baseline and 5 years.

Panel A	RYGB adolescents							Control adolescents		RYGB vs. Control adolescents		
	Raw data				Within group (RYGB Adolescents) mixed-model change			Raw data		Between group mixed-model difference		
	Baseline		5 years		Baseline to 5 years			5 years		5 years		
Variable	Mean (SD)	n	Mean (SD)	n	Mean change	95% CI	p- value	Mean (SD)	n	Mean difference	95% CI	p-value
Height (cm)	170·8 (9·3)	81	172·3 (9·4)	81	1·48	0·9 to 2·1	<0·001	173·0 (10·0)	53	−0·75	−4·2 to 2·7	0·666
Weight (kg)	132·8 (22·1)	81	96·0 (22·2)	81	−36·8	−40·9 to −32·8	<0·001	133·3 (28·9)	53	−37·21	−46·4 to − 28·0	<0·001
BMI (kg/m^2)	45·5 (6·1)	81	32·3 (6·3)	81	−13·14	−14·5 to −11·8	<0·001	44·6 (9·5)	53	−12·26	−15·2 to − 9·3	<0·001
HbA1c (mmol/mol)	35·1 (3·9)	80	33·5 (3·8)	65	−1·56	−2·5 to −0·6	0·002	35·3 (10·6)	37	−1·8	−5·4 to 1·8	0·32
Fasting plasma glucose (mmol/L)	5·1 (0·5)	80	4·8 (0·4)	36	−0·33	−0·5 to −0·1	0·001	5·2 (0·7)	18	−0·45	−0·8 to −0·1	0·009
Fasting capillary glucose (mmol/L)	5·6 (0·5)	78	5·2 (0·5)	73	−0·35	−0·5 to −0·22	0·001	5·8 (2·4)	16	−0·6	−1·8 to 0·6	0·34
Fasting plasma insulin (pmol/L)	216·7 (122·4)	79	65·0 (34·2)	75	−151·42	−173·3 to − 129·5	<0·001	182·8 (122·6)	37	−117·81	−158·3 to − 77·3	<0·001
Triglycerides (mmol/L)	1·3 (0·6)	80	0·9 (0·3)	76	−0·39	−0·5 to −0·3	<0·001	1·4 (0·8)	41	−0·47	−0·7 to −0·2	<0·001
LDL (mmol/L)	2·6 (0·7)	81	2·2 (0·7)	76	−0·46	−0·6 to −0·3	<0·001	3 (0·8)	41	−0·88	−1·2 to −0·6	<0·001
HDL (mmol/L)	1·1 (1·1)	81	1·6 (0·5)	75	0·49	−0·4 to 0·6	<0·001	1·0 (0·3)	42	0·55	0·4 to 0·7	<0·001
Systolic blood pressure (mmHg)	124·6 (12·3)	78	113·2 (10·7)	72	−11·55	−14·0 to −9·1	<0·001	121·4 (11·4)	40	−8·18	−12·5 to − 3·8	<0·001
Diastolic blood pressure (mmHg)	76·9 (9·8)	78	69·4 (9·9)	72	−7·4	−10·2 to −4·6	<0·001	77·7 (10·0)	40	−8·28	−12·2 to − 4·4	<0·001
hsCRP (mg/L)	7·2 (5·9)	75	1·8 (2·2)	77	−5·41	−7·4 to −3·5	<0·001	7·9 (6·9)	39	−6·09	−8·3 to −3·9	<0·001
ALT (μkat/L)	0·6 (0·4)	80	0·3 (0·2)	76	−0·35	−0·4 to −0·3	<0·001	0·4 (0·3)	42	−0·16	−0·3 to −0·1	<0·001
AST (μkat/L)	0·5 (0·2)	80	0·4 (0·2)	76	−0·09	−0·1 to −0·0	0·002	0·4 (0·2)	41	−0·04	−0·1 to 0·0	0·25
Haemoglobin (g/L)	139·3 (12·3)	78	127·7 (17·4)	77	−11·69	−15·6 to −7·8	<0·001	141·9 (14·4)	42	−14·17	−20·1 to − 8·3	<0·001

Per protocol data (crossovers excluded). RYGB, Roux-en-Y gastric bypass; SD, standard deviation; n, number of patients; CI, confidence interval; BMI, body mass index; HbA1c, glycated haemoglobin; LDL, low-density lipoprotein; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; ALT, alanine transaminase; AST, aspartate transaminase.

Table 3

Prevalence and remission of CV risk factors at baseline and 5 years.

Panel B	RYGB Adolescents						p-value	Control Adolescents		p-value
Variable	Baseline, n		5 years		Resolution§		RYGB Baseline vs. 5 years	5 years		RYGB vs. Controls at 5 years
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)		n	% (95% CI)	
T2DM	3/81	3·7 (0·8 to 10·4)	0/79	0·0 (0·0 to 4·6)	3/3	100·0 (29·2 to 100·0)	0·250	1/44	2·3 (0·1 to 12·0)	0·372
Disturbed glucose homeostasis	22/81	27·2 (17·9 to 38·2)	6/79	7·6 (2·8 to 15·8)	18/21 *	85·7 (63·7 to 97·0)	0·001	7/44	15·9 (6·6 to 30·1)	0·098
Elevated HbA1c	10/80	12·5 (6·2 to 21·8)	6/65	9·2 (3·5 to 19·0)	5/8 *	62·5 (24·5 to 91·5)	0·727	6/37	16·2 (6·2 to 32·0)	0·345
Impaired fasting plasma glucose	16/80	20·0 (11·9 to 30·4)	0/36	0·0 (0·0 to 9·7)	13/13 *	100·0 (75·3 to 100·0)	0·003	2/18	11·1 (1·4 to 34·7)	0·107
Elevated fasting plasma insulin	56/79	70·9 (59·6 to 80·6)	3/76	3·9 (0·8 to 11·1)	49/52 *	94·2 (84·1 to 98·8)	<0·001	17/37	45·9 (29·5 to 63·1)	<0·001
Dyslipidaemia	56/81	69·1 (57·9 to 78·9)	11/76	14·5 (7·5 to 24·4)	43/52 *	82·7 (69·7 to 91·8)	<0·001	30/41	73·2 (57·1 to 85·8)	<0·001
Elevated LDL	13/81	16·0 (8·8 to 25·9)	0/76	0·0 (0·0 to 4·7)	13/13	100·0 (75·3 to 100·0)	<0·001	9/41	22·0 (10·6 to 37·6)	<0·001
Elevated triglycerides	25/80	31·3 (21·3 to 42·6)	0/76	0·0 (0·0 to 4·7)	22/22 *	100·0 (84·6 to 100·0)	<0·001	10/41	24·4 (12·4 to 40·3)	<0·001
Low HDL	41/81	50·6 (39·3 to 61·9)	11/75	14·7 (7·6 to 24·7)	28/37 *	75·7 (58·8 to 88·2)	<0·001	27/42	64·3 (48·0 to 78·4)	<0·001
Elevated blood pressure	12/78	15·4 (8·2 to 25·3)	2/72	2·8 (0·3 to 9·7)	12/12	100·0 (73·5 to 100·0)	0·013	4/39	10·3 (2·9 to 24·2)	0·182
Elevated systolic blood pressure	11/78	14·1 (7·3 to 23·8)	0/72	0·0 (0·0 to 5·0)	11/11	100·0 (71·5 to 100·0)	0·001	2/39	5·1 (0·8 to 17·3)	0·121
Elevated diastolic blood pressure	4/78	5·1 (1·4 to 12·6)	2/72	2·8 (0·3 to 9·7)	4/4	100·0 (39·8 to 100·0)	0·688	4/39	10·3 (2·9 to 24·2)	0·182
Elevated hsCRP	65/75	86·7 (76·8 to 93·4)	19/77	24·7 (15·6 to 35·8)	45/61 *	73·8 (60·9 to 84·2)	<0·001	32/39	82·1 (66·5 to 92·5)	<0·001
Elevated liver enzymes	25/81	30·9 (21·1 to 42·1)	4/76	5·3 (1·5 to 12·9)	23/25	92·0 (74·0 to 99·0)	<0·001	8/44	18·2 (8·2 to 32·7)	0·030
Elevated ALT	24/80	30·0 (20·3 to 41·3)	2/76	2·6 (0·3 to 9·2)	23/24	95·8 (78·9 to 99·9)	<0·001	7/42	16·7 (7·0 to 31·4)	0·010
Elevated AST	9/80	11·3 (5·3 to 20·3)	4/76	5·3 (1·5 to 12·9)	9/9	100·0 (66·4 to 100··0)	0·267	3/41	7·3 (1·5 to 19·9)	0·695
Anaemia	8/78	10·3 (4·5 to 19·2)	25/77	32·5 (22·2 to 44·1)	5/7 *	71·4 (29 to 96·3)	0·002	3/42	7·1 (1·5 to 19·5)	0·001

Per protocol data (crossovers excluded). RYGB, Roux-en-Y gastric bypass; SD, standard deviation; n, number of patients; CI, confidence interval; T2DM, type 2 diabetes mellitus; HbA1c, glycated haemoglobin; LDL, low-density lipoprotein; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; AST, aspartate transaminase; ALT, alanine transaminase.

Definitions: T2DM, fasting plasma glucose ≥7 mmol/L, or HbA1c ≥45 mmol/mol); disturbed glucose homeostasis, fasting plasma glucose ≥5·5 mmol/L but <7 mmol/L, HbA1c ≥39 mmol/mol but <45 mmol/mol, or fasting capillary glucose ≥6·1 mmol/L but <7·0 mmol/L; elevated HbA1c, ≥39 mmol/mol; impaired fasting plasma glucose, ≥5·6 mmol/L; elevated fasting plasma insulin, ≥139 pmol/L; dyslipidaemia, elevated LDL or triglycerides, or low HDL; elevated LDL, if <21 years ≥3·37 mmol/L, if ≥21 years ≥4·14 mmol/L; elevated triglycerides, if <21 years ≥1·47 mmol/L, if ≥21 years ≥2·26 mmol/L; elevated HDL, if <21 years ≤1·04 mmol/L, if ≥21 years males ≤1·04 mmol/L, females ≤1·29 mmol/L; elevated blood pressure, elevated systolic or diastolic blood pressure; elevated systolic and diastolic blood pressure, if <18 years ≥95th percentile for age, sex and height, if ≥18 years systolic ≥140 mmHg or diastolic ≥90 mmHg; elevated hsCRP, ≥2mg/L; elevated liver enzymes, elevated AST or ALT; elevated ALT, ≥0.7 µkat/L; elevated AST, ≥0.7 µkat/L; anaemia, haemoglobin males <110 g/L, females <100 g/L;

§ see supplementary material for definition of resolution;

* number in resolution calculation lower than baseline denominator owing to missing data.

Table 4

Adverse outcomes in adolescents following Roux-en-Y gastric bypass across 5 years.

Panel A		
Serious adverse events		**n (%)**
All surgery		20[*] (25)
Laparoscopy	Small bowel obstruction[§]	11 (14)
Cholecystectomy	Gallstones	9 (11)
Laparotomy	Severe abdominal pain	1 (1)
Blood / iron transfusion	Severe anaemia[^]	2 (2)
Observation and investigation only	Abdominal pain	9 (11)
Psychiatric assessment	Drug abuse[#]	6 (7)

Panel B	
Other adverse outcomes	**n (%)**
Anaemia	25/77 (32)
Low Vitamin D	2/73 (3)
Low Vitamin B12	16/73 (22)
Low ferritin or iron	51/77 (66)
Assessment by eating disorder team[§]	1/81 (1)

Adverse outcomes among adolescents undergoing Roux-en-Y gastric bypass for severe obesity. Panel A – events involving admission to hospital; Panel B, events not requiring hospital admission.

[*] 21 procedures in 20 patients;

[§] obstruction caused by internal herniation or adhesions;

[#] narcotic abuse requiring medical referral or intervention;

[^] anaemia requiring admission for iron therapy or blood transfusion;

[§] individual was referred for assessment but was never diagnosed with an eating disorder; definitions and thresholds are provided within the supplementary data.