Obesity in Adolescents and Youth: The Case for and against Bariatric Surgery

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Obesity and its associated sequelae of hypertension, dyslipidemia, cardiovascular disease, type 2 diabetes mellitus (T2DM), disturbances of reproduction, sleep apnea, and nonalcoholic steatohepatitis has been termed the plague of the 21st century and is increasing throughout the world in both adults and children.[1-12]

In a cohort of over 3000 children in the US aged 2 to 19 years, nationally representative data on the prevalence of obesity and its severity from the National Health and Nutrition Examination Survey indicate a continuous increase in the overall trend of obesity, defined as body mass index (BMI) >95th percentile for age, from 16.8% (95% CI 14.2-19.8) in 2007-2008 to 18.5% (95% CI 15.8-21.3) by 2015-2016. The prevalence of severe obesity in childhood defined as BMI >120% of the 95th percentile for age, also showed an increase from 4.9% to 5.6%.[13]

Reflecting these trends in obesity, the incidence of T2DM (number of new cases per 100 000 youth/year) also has increased significantly, most dramatically in the minority populations (Native American Indians, Non-Hispanic Black, Hispanic, and Pacific Islanders) in whom rates have almost doubled over the decade 2002-2012.[13-15]

The complications associated with childhood obesity include psycho-social dimensions of poor self-esteem, discrimination, and lower quality of life measures, in addition to the metabolic and medical associations listed above and are costly in terms of healthcare expenditures; it is estimated that excess medical costs because of overweight adolescents are more than $14 billion per year.[16] However, avoidance of obesity, or prevention, or delay of its complications has generally proven only modestly effective and in some instances, ineffective.[17-21]

For example, the Treatment Options to prevent Type 2 Diabetes in Adolescents and Youth (TODAY) study [9,12] demonstrated only modest effects of life style interventions on dysmetabolic measures and addition of metformin or rosiglitazone, agents effective in many adults, had little effect in delaying the appearance of diabetes in the adolescents."[12] Persistence of obesity, noted at age 7 years, beyond puberty increases the risk of adult T2DM[15]; indeed, some severely obese children manifest diabetes as adolescents. Sample estimates indicate that there are more than 190 000 adolescents aged <20 years with either type 1 diabetes mellitus or T2DM in the US, for an overall prevalence of 1:433 children; T2DM is more prevalent in severely obese minority populations.[15] Nearly one-half of all new cases of diabetes in teens are now known to be T2DM and it is expected to supersede type 1 diabetes as the most common cause of diabetes in adolescents.[8,10,12,15,22]

BMI	Body mass index
QOL	Quality of life
TODAY	Treatment Options to prevent Type 2 Diabetes in Adolescents and Youth
T2DM	Type 2 diabetes mellitus

Unique Aspects of T2DM in Adolescents

There are several unusual features of T2DM in youth vs adults. First, there is a more rapid decline in β-cell function, 20%-35% per year in teens vs 7%-11% per year in adults, even with aggressive medical therapy, so that a requirement for insulin becomes apparent earlier.[23] Indeed about 6% of adolescent patients with T2DM present with diabetic ketoacidosis at diagnosis, reflecting more severe insulin deficiency at the outset. Second, there is an accelerated tempo in the development of complications associated with diabetes mellitus; impaired renal function manifest as albuminuria occurs in ~6% within 5 years of diagnosis and about 2.3% have end-stage renal failure by 10 years after diagnosis. Microvascular changes (eg, retinopathy) also appear earlier; reduction of brain volume with microstructural changes in white matter and decreased cognitive function have been reported.[23] In the TODAY study, those with a BMI ≥35 kg/m^2 demonstrated rapid progression of cardiovascular risk factors despite treatment; hypertension tripled over 4 years from 11% to 34%; microalbuminuria increased from 6% to 17% within 3 years; high-risk low-density lipoprotein cholesterol (low-density lipoprotein cholesterol >130 mg/dL or taking medication) increased from 4.5% to 11% after 3 years.[9] As previously noted, life style intervention and metformin failed and the introduction of insulin promotes further weight gain.[8,9,12,22,23]

Role of Bariatric Surgery in Adults

Given these challenging obstacles to successful life style interventions and medical treatments, what other options are available? In adults, the American Diabetes Association recommends bariatric surgery in those with BMI of 30 kg/m^2 and poorly controlled diabetes mellitus (BMI 27.5 kg/m^2 in Asian Americans) as the most effective and durable treatment for obesity.

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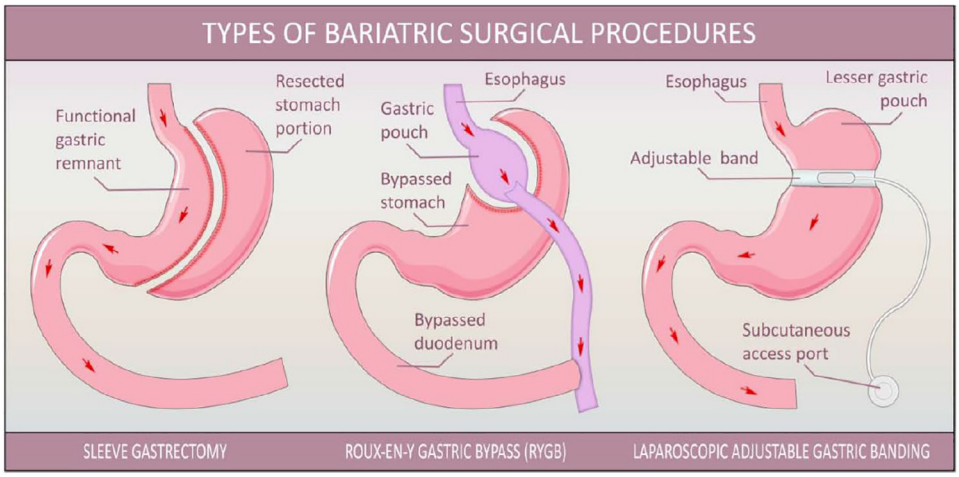

Figure. Simplified diagram illustrating different types of common bariatric surgical procedures; sleeve gastrectomy, Roux-en-Y gastric bypass, and gastric banding.

Clinical practice guidelines for the selection and perioperative, nutritional, and metabolic support for bariatric surgery in these patients have been published.[24] In 2016, there were approximately 216 000 bariatric surgical procedures performed in the US; approximately 58% were gastric sleeve procedures, 18.7% were Roux-en-Y procedures, and only 3.4% were gastric band procedures (**Figure**). Notably, revisions for surgical complications were almost 14% of all operative procedures, and likely contribute to the shift in the type of bypass procedures over the 5 years 2011-2016, which have declined from predominantly gastric banding and Roux-en-Y procedures to predominantly gastric sleeve procedures, as this less complex procedure was anticipated to have fewer post-operative complications .[25] In a recent review, bariatric surgery was considered an effective treatment for severe obesity in adults that results in durable improvement or remission of much obesity-related comorbidity, including sustained weight loss and improved quality of life.[26] In addition, bariatric surgery was considered safe, with mortality comparable with common elective general surgery procedures. Evidence shows that bariatric surgery in adults is superior to conventional medical therapy in improvement of T2DM.[26] However, patients require life-long follow-up and monitoring of nutritional deficiencies; almost all develop deficiencies of vitamin B12, folate, iron, and may also have vitamin D and vitamin C deficiency, and also may continue to have various surgical abdominal issues. Although laparoscopic Roux-en-Y gastric bypass was the most commonly performed bariatric surgical procedure, vertical sleeve gastrectomy is now emerging as a recognized alternative with increasing popularity among all weight loss procedures performed in both adults and adolescents.[25,27] Sleeve gastrectomy has been demonstrated to be relatively safe and equally effective alternative to Roux-en-Y, with shorter duration of operative time for a less complex surgical procedure and with faster postoperative recovery compared with Roux-en-Y.[25,28] Several randomized trials comparing weight loss, remission, and improvement of comorbid conditions in patients undergoing various surgical procedures demonstrated that short- and longer- term outcomes were, in most instances, comparable or equivalent between Roux-en-Y gastric bypass vs sleeve gastrectomy procedures, both being superior to gastric banding.[27-31]

The mechanisms through which the dramatic improvements in weight and metabolic consequences are achieved remain incompletely understood and under intense investigation, but include reduction in volume and calories of food consumed (gastric banding, sleeve gastrectomy, Roux-En-Y procedure), diversion of absorbable surface area (Roux-En-Y), more rapid and effective stimulation of insulin secretion via incretin mediators such as glucagon-like peptide-1 and peptide YY, increased secretion of fibroblast growth factor 19, which regulates bile acid synthesis with effects on glucose and lipid metabolism, and reduction in ghrelin, a hormone predominantly produced in the stomach that normally signals hunger to the brain and increases appetite. After Roux-En-Y procedure, there also is greater extraction of nutrients for glucose production within the remaining gut and other organ specific adaptations characterized by energy consuming processes with repression of the effects of growth hormone receptor signaling.[24,26,32-34]

Potential Role of Bariatric Surgery in Adolescents

Compared with an extensive literature in adults, published reports on the use of bariatric surgery in adolescents are relatively sparse, although increasing in recent years. In a multicenter prospective study of 242 adolescents enrolled in 5 centers in the US, age of subjects was 17 ± 1.6 years (mean ± SEM), BMI 53 kg/m^2, 75% were female, and 72% were Caucasian; 161 subjects underwent Roux-En-Y and 67 sleeve gastrectomy procedures with outcome measures after 3 years focusing on change in weight, coexisting metabolic conditions, cardiometabolic risk factors, quality of life (QOL) measures, and postoperative

Table. Summary of data of weight reduction, comorbidity, and remission rates following bariatric surgery

Number of patients (n) and type of procedures	Study duration, y	Age, y *	BMI†	BMI % reduction	Comorbid condition remission rate					Authors	Year
					T2DM	Prediabetes	Hypertension	Dyslipidemia	Abnormal kidney function		
n = 228 total (RYGB n = 161 gastric sleeve n = 67)	3	17	53	28%	95%	76%	74%	66%	86%	Inge et al[35]	2016
RYGB n = 58	8	17. 1	58.5	29%	89%		67%	48%	—	Inge et al[36]	2017
RYGB n = 81	5	16. 5	45.· 5	29%	100%	86%	92%	83%	—	Olbers et al[37]	2016

RYGB, Roux-en-Y gastric bypass.
Based on results reported in Inge et al[35,36] and Olbers et al[37].
*Mean age in years at the timing of bariatric surgical procedure.
†Baseline BMI in kg/m^2.

complications. Fourteen subjects who had undergone gastric banding were not included in the analysis. The key outcome measures showed a mean weight loss of 27%, remission of T2DM in 95%, remission of abnormal kidney function in 86%, remission of prediabetes in 76%, resolution of elevated blood pressure in 74%, and remission of dyslipidemia in 66%; weight-related QOL indices also improved significantly (**Table**). However, these dramatic improvements after 3 years were associated with hypoferritinemia and/or other micronutrient deficiencies including vitamin B12 in 57% and 13% required 1 or more additional operative procedures.[35] In another study of a prospective follow-up analysis in adolescents with severe obesity undergoing bariatric surgery, Inge et al reported on the outcomes in 74 subjects aged 13-21 years who had Roux-En-Y bariatric surgery procedures 5-12 years after surgery. Of this cohort, 58 were located, eligible, and agreed to follow-up. At baseline age was 17.2 ± 1.7 years, and BMI was 58.5 ± 10.5 kg/M^2. At follow-up 8 ± 1.6 years later, age was 25.1 years and BMI 41.7 kg/m^2, the proportion of subjects with T2DM decreased from 16% at baseline to 2% at follow-up, hypertension decreased to 16% vs 47% at baseline, and dyslipidemia declined from 86% at baseline to 38% at follow up. Mild anemia not requiring treatment was present in 46%, 16% had vitamin B12 deficiency, and secondary hyperparathyroidism because of vitamin D deficiency was found in 45%; all are correctible by supplementation. Thus, Roux-en-Y gastric bypass surgery resulted in substantial and durable weight reduction with cardiometabolic benefits for young adults (**Table**).[36] Similar results were reported from a study in Sweden involving 100 obese adolescents; those undergoing Roux-en-Y gastric bypass (81 subjects) had substantial weight loss over 5 years as well as improvements in comorbidities and risk factors, whereas conventional therapy resulted in further weight gain. However, surgery was associated with nutritional deficiencies, and further surgical procedures as noted in other studies.[37] Bariatric surgery for obese adolescents with comorbidities is also increasingly receiving attention in other countries.[38-40] The objective of this review is to inform pediatricians who care for obese adolescents of the availability of bariatric surgery as an approach that is potentially safe and effective in the management of obesity and its associated comorbid conditions as well as the medical complications that can be anticipated, corrected, and managed. Unfortunately, many pediatricians are reluctant to refer adolescents for bariatric surgery, in part, because of lack of knowledge and concerns regarding the safety and efficacy of these procedures.[41-44]

Cost-Effectiveness of Bariatric Surgery in Adolescents with Severe Obesity

A frequent question is whether the outcome warrants the costs of hospitalization, surgery, and recovery. An assessment of the cost-effectiveness of bariatric surgery in adolescents using results from the Teen-Longitudinal Assessment of Bariatric Surgery study has recently been published. The main outcome measures were quality-adjusted life-years, total costs in US dollars adjusted to 2015-values using the Consumer Price Index, and incremental cost-effectiveness ratios. A willingness-to-pay threshold of $100 000 per quality-adjusted life-year was used to assess cost-effectiveness. Although bariatric surgery incurs substantial initial costs and morbidity, if assessed over a time period of 5 years, bariatric surgery in severely obese adolescents would be cost-effective. Further long-term outcomes studies for adolescents undergoing bariatric surgery are needed to confirm and refine these results.[45]

Which Adolescents Should be Offered Bariatric Surgery?

The Endocrine Society, in conjunction with the European Endocrine Society and the Pediatric Endocrine Society published a Clinical Practice Guideline on the assessment, treatment and prevention of Pediatric Obesity.[46,47] These guidelines suggest and/or recommend:

> *"Against bariatric surgery:*
> *Bariatric surgery should not be performed in preadolescent children, pregnant or breast-feeding adolescents (and those planning to become pregnant within 2 years of surgery), and in any patient who has not mastered the principles of healthy dietary and activity habits and/or has an unresolved substance abuse, eating disorder, or untreated psychiatric disorder".*[47]

Generally speaking, the surgical risk associated with bariatric procedures appears to be comparable with standard elective

surgical procedures, but unfortunately the possibility of requiring additional procedures secondary to complications exists and is substantial. Micronutrient deficiencies resulting from altered absorption may have implications on multiple body systems including but not limited to skeletal system (vitamin D, parathyroid hormone), the nervous system (vitamin B1, B12, iron), as well as the blood (hypoferritinemia). Supplementation of multivitamins and minerals such as iron, vitamins A, vitamin C, 25 hydroxyvitamin D, and B12 and regular monitoring of the potential dietary and micronutrient deficiencies in patients following bariatric surgical procedures is essential. Finally, with the obesity epidemic continuing to involve younger and younger individuals, great caution remains with the implementation of surgical procedures in prepubertal and growing children especially regarding long-term bone mineralization. More data in this age group are needed.[26,35,36]

"For bariatric surgery
Only under the following conditions:

1. *The patient has attained Tanner 4 or 5 pubertal development and final or near-final adult height, the patient has a BMI of 40 kg/m^2 or has a BMI of 35 kg/m^2 and significant, extreme comorbidities.*[47]
2. *Extreme obesity and comorbidities persist despite compliance with a formal program of lifestyle modification, with or without pharmacotherapy; psychological evaluation confirms the stability and competence of the family unit [psychological distress due to impaired QOL from obesity may be present, but the patient does not have an underlying untreated psychiatric illness].*[47]
3. *The patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits.*[47]
4. *There is access to an experienced surgeon in a pediatric bariatric surgery center of excellence that provides the necessary infrastructure for patient care, including a team capable of long term follow-up of the metabolic and psychosocial needs of the patient and family."*[47]

We quote these carefully considered guidelines to emphasize the importance of specialized units capable of providing the surgical, medical, nursing, and psychological expertise under the aegis of clinical investigative trials. The guidelines also recognize the importance of an unstable home environment, history of recidivism, drug or alcohol abuse, established psychiatric disorder, and emotional instability as contraindications for surgery. The surgical procedures are not without risk and a reoperation rate of 10%-20% even in the best hands for Roux-en-Y procedures adds additional risks and costs; the recent trend to gastric sleeve procedure because it is simpler and less complicated seems likely to diminish the reoperation rate. To date, studies and outcomes are of relatively short duration; longer outcomes data are needed to evaluate the benefit/risk ratio in adolescents. The need for well-designed, prospective comparative trials of medical vs surgery to define their respective roles in management of obesity is emphasized in a study that compared outcomes in terms of weight loss, remission of diabetes, or change in HemoglobinA1c (HbA1c) between 30 adolescents who underwent bariatric surgery in the Teen-Longitudinal Assessment of Bariatric Surgery study vs 63 subjects from the TODAY consortia treated medically. In each of the categories assessed, bariatric surgery was significantly superior; however, 23% of the surgical group required some form of reoperation over the succeeding 2 years.[46] It appears that if the recommended guidelines and conditions are met, bariatric surgery offers durable remission and reversal of obesity related-comorbidities, and, in the longer-term, cost effective care in adolescents.

The argument that obesity may and should be recognized as a disease with eventual multiple organ system failure is certainly plausible. The question remains "are we doing enough to manage obesity?" With objective evidence pointing to significant remission rates of T2DM along with remission or improvement in several other comorbidities as well as significant weight loss, bariatric surgery for the appropriate patient in the appropriate facility should be considered as a reliable, effective and economically justifiable therapeutic intervention.

Conclusions

Obesity and associated comorbid conditions are a major threat to our youth, and bariatric surgical procedures represent an effective, substantial, durable, and a long-term cost-effective intervention that may be significantly underutilized in this vulnerable population. Objective evidence of BMI reduction and improvement or resolution in associated comorbid conditions, especially T2DM, suggest that primary care providers should consider referral of obese adolescents to bariatric surgical procedures in recognized centers of excellence. Complications, such as standard surgical risk, the need for lifelong supplementation to prevent or treat dietary deficiencies, implications on bone health, and the possibility of resurgery are reasonable concerns, however, the benefit of bariatric surgical procedures in youth appears to outweigh the risks for the carefully selected patient in the appropriate medical center. Bariatric surgery is likely to become increasingly available as more data on long-term outcomes in larger cohorts become known.[26,36,46] ■

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