

Kidney outcomes three years after bariatric surgery in severely obese adolescents

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A significant number of severely obese adolescents undergoing bariatric surgery have evidence of early kidney damage. To determine if kidney injury is reversible following bariatric surgery, we investigated renal outcomes in the Teen-Longitudinal Assessment of Bariatric Surgery cohort, a prospective multicenter study of 242 severely obese adolescents undergoing bariatric surgery. Primary outcomes of urine albumin-to-creatinine ratio and cystatin C-based estimated glomerular filtration rate (eGFR) were evaluated preoperatively and up to 3 years following bariatric surgery. At surgery, mean age of participants was 17 years and median body mass index (BMI) was 51 kg/m². In those with decreased kidney function at baseline (eGFR under 90 mL/min/1.73m²), mean eGFR significantly improved from 76 to 102 mL/min/1.73m² at three-year follow-up. Similarly, participants with albuminuria (albumin-to-creatinine ratio of 30 mg/g and more) at baseline demonstrated significant improvement following surgery: geometric mean of ACR was 74 mg/g at baseline and decreased to 17 mg/g at three years. Those with normal renal function and no albuminuria at baseline remained stable throughout the study period. Among individuals with a BMI of 40 kg/m² and more at follow-up, increased BMI was associated with significantly lower eGFR, while no association was observed in those with a BMI under 40 kg/m². In adjusted analysis, eGFR increased by 3.9 mL/min/1.73m² for each 10-unit loss of BMI. Early kidney abnormalities improved following bariatric surgery in adolescents with evidence of preoperative kidney disease. Thus, kidney disease should be considered as a selection criteria for bariatric surgery in severely obese adolescents who fail conventional weight management.

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Severe obesity, defined as a body mass index (BMI) > 120% of the 95th percentile or an absolute BMI \geq 35 kg/m², is increasing and now affects 4% to 6% of US children and adolescents.¹⁻³ The American Heart Association recently issued a consensus statement to raise awareness of this growing problem and summarize available treatment options. Considering the limited effectiveness of lifestyle and pharmacologic interventions, use of bariatric surgery has been advocated for appropriately selected adolescents with severe obesity and obesity-related comorbidities.⁴

The obesity epidemic has been paralleled by a proportionate increase in chronic kidney disease (CKD).⁵ Obesity now is recognized as an independent risk factor for CKD, with recent estimates indicating that 24% to 33% of all kidney disease could be related to obesity.⁶ Obese children, moreover, have a significantly higher risk of developing CKD and end-stage renal disease in adulthood.^{7,8} To estimate the prevalence of early kidney disease in severely obese adolescents, we recently conducted a baseline analysis of the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) cohort. Teen-LABS is a prospective observational study of adolescent bariatric surgical patients that aims to understand the broad-ranging outcomes after bariatric surgery. We reported that a concerning number of severely obese adolescents undergoing bariatric surgery had evidence of early kidney disease at baseline before surgery: 17% had albuminuria and 3% had significantly decreased estimated glomerular filtration rate (eGFR).⁹

Despite promising results of bariatric surgery to improve obesity and obesity-related comorbidities,¹⁰ little is known about the potential salutary effect of bariatric surgery on obesity-related kidney disease in adolescents. To determine if early kidney injury that is associated with severe obesity reverses after weight loss surgery, we analyzed kidney outcomes in the Teen-LABS cohort up to 3 years after bariatric surgery. We hypothesized that albuminuria and eGFR would improve postoperatively, with the greatest improvement occurring in those with the most severe kidney abnormalities before undergoing bariatric surgery.

RESULTS

Demographic and clinical characteristics

The mean age at surgery was 17.1 years. Of the 242 subjects, 75.6% were female and 64.9% were non-Hispanic white.

Procedures included Roux-en-Y gastric bypass (gastric bypass) in 66.5%, sleeve gastrectomy in 27.7%, and adjustable gastric band in 5.8%. Clinical characteristics of the cohort at baseline and at the 3-year follow-up evaluation are presented in Table 1. Significant improvements occurred in BMI and other cardiovascular risk factors after bariatric surgery. The median BMI decreased from 50.5 kg/m² at baseline to 36.2 kg/m² at the 3-year follow-up evaluation. Most of this change occurred during the first 6 months postoperatively, after which the median BMI was 38.0 kg/m². Significantly reduced ferritin levels and increases in transferrin levels were evident in the cohort. However, significant improvements were seen in the homeostasis model assessment of insulin resistance, C-reactive protein, and the percentage of participants with dyslipidemia, hypertension, and diabetes. The percentage of participants taking antihypertensive medications also decreased: 22% at baseline compared with 7% at the 3-year follow-up evaluation. Of those taking antihypertensive medications, 59% were taking angiotensin-converting enzyme inhibitors at baseline and 23% at the 3-year follow-up evaluation.

Estimated glomerular filtration rate

The mean (\pm SD) of cystatin C–based eGFR at baseline was 108 \pm 27 ml/min per 1.73 m², and this increased by 6% to 115 \pm 29 ml/min per 1.73 m² at 3 years after surgery ($P = 0.02$). In this severely obese cohort, a low eGFR (<90 ml/min per 1.73 m²) was observed in 24.8% (59 of 238) at baseline and improved to 15.5% (29 of 187) at the 3-year follow-up evaluation ($P = 0.004$). An abnormally high eGFR (≥ 150 ml/min per 1.73 m²) was present in 7.1% (17 of 238) at baseline and in 7.5% (14 of 187) at 3 years ($P = 0.83$).

The 3-year follow-up evaluation of eGFR stratified by baseline level of renal function (<90 vs. ≥ 90 ml/min per 1.73 m²) is presented in Figure 1. The majority of improvement in renal function occurred in those with a baseline eGFR of <90 ml/min per 1.73 m², whose mean (\pm SD) eGFR

was 76 \pm 12 ml/min per 1.73 m². In this group, eGFR improved by 34% to 102 \pm 28 ml/min per 1.73 m² at the 3-year follow-up evaluation ($P < 0.0001$). Improvement in renal function first was detected at the earliest postoperative visits (6–12 months postoperatively), and then remained stable throughout the remainder of the study period. Among the 7 subjects with a baseline eGFR of <60 ml/min per 1.73 m², eGFR improved from 52 \pm 7 ml/min per 1.73 m² at baseline to 98 \pm 32 ml/min per 1.73 m² at 1 year ($n = 6$; $P = 0.03$), 103 \pm 38 ml/min per 1.73 m² at 2 years ($n = 6$; $P = 0.01$), and 94 \pm 48 ml/min per 1.73 m² at 3 years ($n = 5$; $P = 0.08$) of follow-up evaluation. However, those with an eGFR ≥ 90 ml/min per 1.73 m² at baseline did not change significantly over time (118 \pm 21 ml/min per 1.73 m² at baseline and 119 \pm 28 ml/min per 1.73 m² at the 3-year follow-up evaluation; $P = 0.98$). A nonstatistically significant decrease in eGFR also was detected in the small subgroup ($n = 17$) with eGFR ≥ 150 ml/min per 1.73 m² at baseline, for whom the mean eGFR of 162 \pm 16 ml/min per 1.73 m² decreased to an eGFR of 138 \pm 32 ml/min per 1.73 m² at 3 years ($n = 15$; $P = 0.07$).

Albuminuria

Albuminuria was observed in 17.0% (39 of 230) of the cohort at baseline and decreased to 11.0% (19 of 173) at the 3-year follow-up evaluation ($P = 0.06$). Participants with albuminuria at baseline showed a significant improvement in the albumin-to-creatinine ratio (ACR): the geometric mean of the ACR was 74 mg/g (95% confidence interval, 45–121 mg/g) at baseline and decreased to 17 mg/g (95% confidence interval, 10–28 mg/g) at 3 years ($P < 0.0001$). Of these subjects, 69% experienced normalization of albuminuria at the 2-year follow-up evaluation, and 75% experienced resolution of albuminuria at the 3-year follow-up evaluation.

The 3-year follow-up evaluation of the ACR ratios stratified by baseline level of albuminuria is presented in Table 2. Preoperatively, 13.9% (32 subjects) had microalbuminuria and 3.0% (7 subjects) had macroalbuminuria. Among those with microalbuminuria, an 83% reduction in ACR was observed 1 year postoperatively ($P < 0.0001$). The 7 participants with macroalbuminuria at baseline also showed a remarkable improvement during the study period, 3 of whom had complete normalization of urinary protein at the 1-year follow-up evaluation ($P < 0.0001$). Among those with normal levels of urinary albumin at baseline, there was no significant change in the ACR at the 3-year follow-up evaluation, although 11 of these subjects (7.6%) developed incident microalbuminuria at 3 years.

Association of BMI with GFR during the study period

The relationship between BMI and eGFR was investigated at each study time point. At baseline, those with higher BMI values showed a lower eGFR; a strongly negative correlation was observed ($r = -0.34$; $P < 0.0001$). However, this inverse association between BMI and eGFR dissipated postoperatively, and was no longer significant by 2 years

Table 1 | Clinical characteristics at baseline and 3-year follow-up evaluation in the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) cohort

Variable	Baseline (N = 242)	3-year follow-up evaluation (N = 206)	P value
BMI, kg/m ²	50.5 (45.2, 58.3)	36.2 (30.2, 44.9)	<0.0001
Hypertension	104 (43.7%)	29 (15.3%)	<0.0001
Type 2 diabetes	30 (12.6%)	1 (0.6%)	<0.0001
Dyslipidemia	179 (75.2%)	54 (30.0%)	<0.0001
Transferrin, mg/dl	268 (244, 292)	313 (274, 352)	<0.0001
Ferritin, μ g/l	37.0 (23.0, 66.0)	9.0 (5.0, 24.0)	<0.0001
Serum albumin, g/dl	4.1 (3.9, 4.4)	4.3 (4.1, 4.5)	<0.0001
HOMA-IR	5.91 (3.60, 9.98)	1.97 (1.20, 3.32)	<0.0001
hsCRP, mg/l	0.63 (0.30, 1.17)	0.09 (0.03, 0.32)	<0.0001
HbA1c	5.20 (5.00, 5.50)	5.1 (4.9, 5.3)	<0.0001

BMI, body mass index; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment of insulin resistance; hsCRP, high-sensitivity C-reactive protein. Data are presented as medians (25th, 75th percentile) or n (%). P values were generated from generalized linear mixed models analysis.

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