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Gastric Bypass surgery and measured and estimated GFR in women

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Summary

Obesity causes hyperfiltration. Patients lose a substantial amount of weight after bariatric surgery. This weight loss includes a decrease in muscle mass, as evidenced by a decrease in creatinine excretion. Hyperfiltration also improves but is not detected by changes in serum creatinine due to concurrent decreases in creatinine generation.

Keywords

bariatric surgery; creatinine generation; estimated GFR; gastric bypass; iothalamate clearance; obesity; proteinuria

Obesity (body mass index (BMI) greater than 30 kg/m²) is associated with glomerular hyperfiltration, glomerular hypertrophy, and proteinuria, all potentially harmful ¹. Although bariatric surgery can achieve sustained long-term weight loss, is recommended by consensus guidelines ², and is associated with overall decreased mortality ³, the renal effects of this acute weight loss on glomerular hyperfiltration are not clearly established, and the accuracy of the equations that are used to estimate GFR (eGFR) before and after the procedure is unclear.

Subjects with a BMI in excess of 40 kg/m² undergoing bariatric surgery were recruited ⁴. Comprehensive evaluation including 24-hour urine collection, serum creatinine, and dietary intake assessment by food frequency questionnaire ⁷ were conducted at an outpatient visit prior to, and at 6 and 12 months after surgery. eGFR was calculated by the 2009 CKD-EPI equation ⁵, while GFR was measured (mGFR) using renal iothalamate clearance ⁸. Body surface area was estimated from height and weight ⁶.

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Contributions: research idea and study design: MLC, RK, JCL; data acquisition: MLC, RK, JCL; data analysis/interpretation: EB, MLC, RK, JCL, ADR, MGS; statistical analysis: EB; supervision or mentorship: N/A. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. JCL takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Statistical analysis employed as a mixed effects models to test for an overall (fixed) time effect (baseline, 6 months, 12 months) with random repeated subject effects. Paired t-tests were also done to assess specific differences from baseline. Associations between quantitative factors were done using Pearson's correlation coefficient. Multiple readings were corrected using generalized estimating equations. Analyses were done using SAS, version 9.1 (SAS institute, Cary, NC). Continuous data are presented as mean plus or minus standard deviation.

Eleven Caucasian women aged 50 ± 12 years (range 28–68 years) participated (Table 1), 9 of whom underwent standard RYGB and 2 a biliopancreatic diversion/ duodenal switch. Preoperative BMI was 46 ± 5 kg/m² and 2 patients had diabetes. BMI decreased to 33 ± 5 and 28 ± 2 kg/m² at 6 and 12 months after surgery ($P < 0.001$). At baseline 7 of 11 patients required a median of 1 (0:2.5; p25:p75) antihypertensive medications, while at 12 months only 4 of 11 required 0 (0:1) agents ($p < 0.05$). Baseline diabetes in 2 patients (on metformin only) resolved by 12 months. Serum creatinine decreased slightly, but not significantly, while urinary creatinine excretion fell from 1342 ± 434 mg/24h to 1019 ± 213 and 1035 ± 255 mg/24h at 6 and 12 months, respectively ($P < 0.05$ vs baseline for both; Table 1). Therefore, creatinine and iothalamate clearance decreased by 22 and 31 ml/min, respectively ($p = 0.2$ and 0.02) (Figure 1). Urine albumin excretion fell slightly (4 mg) at 12 months ($P = 0.4$) (Figure S1).

Overall, mGFR correlated with urinary creatinine excretion ($r = 0.69$, $p < 0.001$, Figure S2A), more than with weight ($r = 0.48$, $p = 0.005$; Figure S2B). The large fall in creatinine excretion associated with a decrease in serum creatinine and consequent rise in eGFR ($+10.3$ ml/min/1.73 m², $p = 0.2$). However, BSA corrected mGFR fell after RYGB (10 ml/min/1.73m²), while BSA corrected eGFR slightly increased (6 ml/min/1.73m², Figure S3A). Thus eGFR underestimated GFR at baseline, but overestimated it postoperatively.

Total calorie and protein intakes decreased postoperatively (Table 1). Urinary sodium excretion, a direct reflection of dietary intake, and sulfate and uric acid excretions, correlates of dietary protein intake, were all less after bariatric surgery. The baseline to 12 month decrease in protein intake did not correlate significantly with the decrease in GFR ($r = 0.13$, $p = 0.5$) or the decrease in sodium intake ($r = 0.13$, $p = 0.5$). Furthermore, dietary protein did not correlate with urinary creatinine excretion ($r = 0.10$; $P = 0.5$).

Therefore, this prospective cohort study demonstrates that mGFR fell in a cohort of female patients during the first year after bariatric surgery. Importantly, serum creatinine and eGFR calculated from serum creatinine did not detect this change in kidney function because of a large decrease in creatinine generation. Although volume depletion may have contributed to the postoperative fall in mGFR, especially at six months, by 12 months urine volume and sodium both rebounded close to baseline values yet lower mGFR persisted (Table 1). Our data also suggest that urinary creatinine excretion has a stronger effect on GFR than weight (Figure S2). Although not always recognized, morbidly obese persons often have larger amounts of body fat and muscle mass. Thus, metabolism related to increased muscle mass may be a more important determinant of glomerular filtration than metabolism related to adipose tissue. These changes in muscle mass relative to body weight also have important

implications on the use of the equations used to estimate GFR. Pre-operatively the CKD EPI equation significantly underestimated GFR in this obese population, while it overestimated GFR when the patients lost weight and muscle mass postoperatively.

The primary limitation of the current study is the small number of subjects and the fact that all were female. As such these findings should be validated in larger cohorts containing both men and women. However, a strength is the detailed information available over the first year after surgery, including mGFR at three time points, 24-hour urine collections, and matched quantitative dietary information.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Changes in measured GFR
Each line is an individual patient.

Table 1

Patient characteristics at baseline, and 6 and 12 months after bariatric surgery

	Baseline	6 mo	12 mo
Female/male	11/0	-	-
Age (y)	49.5 (11.5)	-	-
Diabetes (Y/N)	2/9	-	-
Hemoglobin A1C (non- diabetics)	5.4 (0.3)	5.0 (0.5)	5.2 (0.5)
Hemoglobin A1C (diabetics)	9.1 (3.7)	6.2 (0.8)	6.6 (1.3)
Hypertension (Y/N)	7/4	-	-
Weight (kg)	121.2 (18.4)	87.1 (18.2)**	75.7 (9.2)**
BMI (kg/m ²)	45.7 (5.0)	32.5 (5.2)**	28.4 (2.0)**
Systolic BP	124 (13)	120 (16)	118 (10)
Diastolic BP	70 (8)	69 (10)	69 (11)
Serum creatinine (mg/dl)	0.8 (0.2)	0.8 (0.1)	0.7 (0.1)
Urine creatinine (mg/24 h)	1342 (434)	1019 (213)	1035 (255)
Creatinine clearance (ml/min)	120 (64)	95 (30)	98 (27)
Iothalamate clearance (ml/min)	121 (32)	93 (34)	90 (24)*
Uncorrected CKD EPI eGFR (ml/min)	108 (28)	102 (29)	94 (20)
Adjusted iothalamate clearance (ml/min/1.73 m ²)	95 (26)	83 (22)	85 (20)
CKD EPI eGFR (ml/min/1.73m ²)	84 (20)	92 (19)	90 (16)
Urine albumin (mg/24 h)	20.5 (10.4)	14.8 (11.4)	17.1 (10.9)
Food Frequency Questionnaire			
Calories (kcal/24 h)	2248 (816)	1209 (795)*	1509 (784)*
Carbohydrates (g/24 h)	285 (116)	157 (114)*	200 (130)*
Fat (g/24 h)	79.5 (35)	39 (25)*	51 (25)*
Protein (g/24 h)	108 (51)	65 (42)	71 (38)
Sugar (g/24 hrs)	129 (75)	90 (79)*	105 (87)
Diet-dependent urine variables			
Urine Sodium (mEq/24 h)	170 (104)	94 (40)*	136 (60)
Urine Sulfate (mmol/24 h)	23 (12)	11 (5)*	14 (6)*
Urine Uric Acid (mg/24 h)	670 (360)	360 (129)*	404 (135)*
Urine Phosphorous (mg/day)	897 (417)	446 (172)*	553 (168)*
Urine Volume (ml/24 h)	2091 (768)	1317 (540)*	1596 (569)

Values expressed as mean (SD)

* P< 0.05 vs baseline

** P<0.001 vs baseline