Item S1. Detailed methods and supplementary results.

Methods

Patients: This prospective cohort study was conducted pre and post bariatric surgery to examine the impact of weight loss on study outcome measures in obese CKD patients. All patients who had serum creatinine >1.3 mg/dl and were scheduled to undergo bariatric surgery between September 2011 and January 2013 at the Cleveland Clinic were considered for inclusion. Demographic characteristics (age, gender and race), comorbidities (e.g. type 2 diabetes, hypertension, etc.), and medication use were determined.. Patients came to the Clinical Research Unit before and 3, 6 and 12 months after surgery for study tests. Patients were provided both verbal and written informed consent documents approved by our Institutional Review Board.

Bariatric Surgery: Laparoscopic sleeve gastrectomy, laparoscopic adjustable gastric banding, and laparoscopic RYGB were performed using standard techniques.

Body Composition: Anthropometric measures (height, weight, and waist circumference) were measured by standard techniques, and body mass index (BMI) was calculated. Whole body fat mass (FM) and fat-free mass (FFM) was measured by dual-energy X-ray absorptiometry (model iDXA; GE Healthcare - Lunar, Madison, WI).

Insulin Resistance, Inflammation and Adipokine Measures: A 75 g oral glucose tolerance test (OGTT) was performed after an overnight fast. Fasting samples were drawn to determine initial glucose, insulin, leptin, and total and HMW adiponectin concentrations. Following baseline draws, a 75 g glucose drink was ingested within a 10-minute period, and blood samples were collected at 30, 60, 90, 120 and 180 minutes after ingestion. Plasma glucose was determined immediately on a YSI 2300 STAT Plus analyzer (Yellow Springs, OH). The remaining samples

were stored at -80ºC for subsequent substrate analysis. Plasma insulin was determined via radioimmunoassay (Millipore, Billerica, MA). Insulin sensitivity was determined from the homeostasis model assessment- insulin resistance (HOMA-IR) and Matsuda index. Fasting high sensitive C-reactive protein (hs-CRP), plasma leptin, and total and high molecular weight (HMW) adiponectin was analyzed via ELISA (Millipore, Billerica, MA). All blood samples were measured in duplicate, and each participant's pre- and post-intervention samples were batch-analyzed to minimize inter-subject variability.

*Kidney function measure*s: Iothalamate GFR: ^{125}I-sodium iothalamate GFR determination was performed at our institution. Briefly, patients received a water load before the test. ^{125}I-sodium iothalamate (25 μCu; Glofil; Questor Pharmaceuticals, Union City, CA) was injected subcutaneously without epinephrine. Baseline urine and blood samples were obtained. A voluntary-voided urine sample was discarded, followed by one timed clearance urine collection. Blood samples were drawn before and after each urine collection. Isotope activity was determined by gamma counting of 0.5 ml of plasma or urine on a Packard Minaxi 5000 series counter (Perkin Elmer Life Sciences, Downers Grove, IL). The counts in each period were the average of the samples for each clearance period. The mean iGFR was calculated with and without standardizing to body surface area (BSA, 1.73 m^2) using the Dubois and Dubois formula.

Serum creatinine, Cystatin C and β-2-microglobulin: Serum creatinine measurements for the study population were performed in the same clinical laboratory, which used integrated database management system–traceable samples to minimize calibration bias. From fasting blood collections, Cystatin C and β-2-microbolulin were analyzed as potentially novel biomarkers for

renal function. Plasma Cystatin C was measured using a particle enhanced immunoturbidimetric assay. β-2-microglobulin was measured using an immunoturbidimetric assay (Roche). Both assays were run on the Roche Cobas c311 analyzer, a high throughput chemistry analyzer.

Quality of Life: Kidney Disease and Quality Of Life (KDOQL-36) was administered before and 12 month after bariatric surgery.

Statistical Analysis

Fifteen eligible patients were enrolled and 13 completed the 12 month follow up visit. Two subjects did not come for follow-up visits at one year. As a result, only those with follow-up data were included in the analysis. We described patient characteristics and medication intake as N (%), and summarized continuous variables with medians and interquartile ranges. The change in values (kidney function measures, adipokines, insulin resistance and weight loss) from baseline to 12 months post-surgery was evaluated using the Wilcoxon signed rank test. We evaluated the change in medication use from baseline to end of study with McNemar's test. Spearman correlations were used to determine associations between the change in iGFR (adjusted and unadjusted), other renal function markers (serum creatinine, cystatin C and β-2-microglobulin) and the changes in metabolic markers (e.g. leptin, adiponectin and insulin resistance). Tests of hypotheses were carried out at a significance level of $p < 0.05$. Data analyses were conducted using Unix SAS version 9.2 (SAS Institute, Cary, NC), and graphs were created using R 3.0.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Table: Kidney function measures before, 3 month, 6 months and 12 months after surgery (n=13)

Variable	Baseline Median [IQR]	3-month Median [IQR]	6-month Median [IQR]	12-month Median [IQR]
Serum creatinine (mg/dl)	1.6 [1.5, 1.8]	1.3 [1.2, 1.6]	1.4 [1.2, 1.7]	1.4 [1.2, 1.6]
$eGFR_{cr}$ (ml/min)	47.7 [37.4, 52.4]	55.9 [41.8, 71.3]	58.8 [41.7, 65.3]	52.3 [45.1, 63.8]
$eGFR_{cr}$ (ml/min/1.73 m^2)	30.5 [26.8, 34.5]	40.2 [33.0, 46.8]	37.8 [33.7, 48.1]	36.5 [35.9, 44.8]
mGFR (ml/min)	82.0[60.9,89.7]	84.6 [58.9, 108.2]	74.1 [60.5, 113.1]	80.5 [63.0, 111.5]
mGFR (ml/min/1.73 m^2)	50.0[44.0,58.0]	65.5 [40.0, 75.5]	60.5 [45.0, 82.5]	64.0 [48.0, 87.0]
24 hr Proteinuria (g)	0.60[0.16,1.6]	0.43 [0.16, 1.2]	0.75 [0.16, 1.7]	0.43 [0.16, 0.85]

Table: Changes in kidney function measures before and 12 months after RYGB surgery (n=7)

Variable*	Baseline Median[IQR]	12 month Median[IQR]	Change in variable Median[IQR]	p-Value
Serum creatinine (mg/dl)	1.8 [1.3, 2.0]	1.6 [1.08, 1.7]	-0.30 [-0.39, -0.08]	0.05
Cystatin C (mg/dl)	1.9 [1.8, 2.0]	2.0 [1.5, 2.0]	0.03 [-0.33, 0.13]	0.9
β2 microglobulin (mg/dl)	3.5 [3.4, 4.4]	3.6 [2.8, 4.2]	0.00 [-0.70, 0.40]	0.88
$eGFR_{cr}$ (ml/min)	49.4 [33.7, 55.6]	48.7 [41.2, 71.0]	11.3 [0.77, 18.0]	0.05
$eGFR_{cr}$ (ml/min/1.73 m^2)	30.1 [24.5, 43.7]	36.5 [35.5, 58.0]	11.0 [3.9, 17.4]	0.02
$eGFR_{cys}$ (ml/min)	34.0 [31.0, 37.5]	32.8 [30.3, 46.2]	-0.87 [-3.0, 11.6]	0.9
$eGFR_{cys}$ (ml/min/1.73 m^2)	24.0 [22.4, 29.0]	28.9 [24.6, 34.9]	1.01 [0.57, 11.7]	0.03
$eGFR_{Cr\text{-}cys}$ (ml/min)	40.1 [31.7, 47.2]	36.4 [31.1, 57.2]	3.3 [-1.8, 14.7]	0.16
$eGFR_{cr\text{-}cys}$ (ml/min/1.73 m^2)	25.5 [24.9, 31.8]	30.6 [26.8, 46.0]	5.5 [1.9, 14.4]	0.02
mGFR (ml/min)	76.3 [60.9, 101.7]	80.5 [50.8, 117.6]	-0.98 [-10.2, 17.4]	0.81
mGFR (ml/min/1.73 m^2)	50.0 [44.0, 80.0]	69.0 [40.0, 92.0]	9.0 [-4.0, 22.0]	0.22
24 hr Proteinuria (g)	1.3 [0.25, 1.7]	0.85 [0.32, 2.0]	-0.03 [-0.56, 0.54]	0.88

*Wilcoxon signed rank test