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Bariatric Surgery, Kidney Function, Insulin Resistance, and Adipokines in Patients With Decreased GFR: A Cohort Study

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To the Editor

Bariatric surgery induces long-term, sustainable weight loss and improves type 2 diabetes and hypertension, thereby contributing to lower mortality[1–3]. The resulting weight loss also improves glomerular hyperfiltration and albuminuria[4,5]. However, the conclusion that bariatric surgery improves kidney function have been based on using only estimated GFR or 24-hour creatinine clearance in those with CKD[6,7]. In this prospective cohort study, we directly measured kidney function (via measured GFR) in obese individuals with reduced GFR following bariatric surgery and investigated metabolic mechanisms that might account for the effects of weight loss on changes in kidney function.

Fifteen patients undergoing bariatric surgery who had serum creatinine >1.3 mg/dl were included; 13 completed the last follow-up. Patients came to the Clinical Research Unit before and 3, 6, and 12 months after surgery to assess body composition, lipid, metabolic (oral glucose tolerance, adipokines, inflammatory markers), kidney function, and QoL parameters (Table 1; detailed methods in Item S1). Changes from baseline to 12 months

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Author contributions: Research area and study design: SDN, JPK, PRS; data acquisition: SDN, SKM, JPK, PRS; data analysis and interpretation: SDN, SKM, SA, SRK, JPK, PRS. 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. SDN 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 have been explained.

Supplementary Material

Item S1: Detailed methods and supplementary results.

Note: The supplementary material accompanying this article (doi:_____) is available at www.ajkd.org

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postsurgery were evaluated using the Wilcoxon signed rank test. Spearman correlations were used to determine associations between the change in mGFR, other kidney function markers, and the changes in metabolic markers.

Patients underwent Roux-en-Y gastric bypass (n = 7), laparoscopic adjustable gastric banding (n = 3), or laparoscopic sleeve gastrectomy (n = 3). Median age was 56 (IQR, 49–63) years, with 92% males and 77% Caucasian. All included patients had hypertension and hyperlipidemia and most had type 2 diabetes. At baseline, median unadjusted and BSA-adjusted mGFR were 82 (IQR, 60.9–89.7) ml/min and 50 (IQR, 44.0–58.0) ml/min/1.73 m^2, respectively.

Twelve months after surgery, BMI, waist circumference, fat mass, and fat-free mass decreased significantly, along with some improvement in lipid profile and SF-12 physical composite scores. Matsuda Index and total/HMW adiponectin also increased, while HOMA-IR, plasma leptin, and hs-CRP levels decreased (Table 1). These anthropometric and metabolic changes corresponded with improvements in most kidney disease measures. Although unadjusted mGFR did not change significantly, there was a significant improvement in BSA-adjusted mGFRs at 3-, 6- and 12-months' follow-up (Item S1). Serum cystatin C and B2M levels did not change at 12 last follow-up (Table 1). Item S1 reports a sensitivity analysis focusing on the Roux-en-Y gastric bypass patients. Change in kidney function (both adjusted and unadjusted mGFR) correlated with leptin and B2M level changes (Table 2), while change in BMI and fat mass did not correlate with kidney function and metabolic parameters.

Our results suggest potential benefits of bariatric surgery and the variations among the different measures of kidney function in those with reduced GFR. The metabolic effects of gastric bypass are well known; as expected, we noted improvements in metabolic parameters with bariatric surgery. We speculate that the absence of decline in kidney function over the course of our study may be a potential benefit in those with reduced GFR, but the lack of control group precludes definitive conclusions[8]. With rapid weight loss during the first few months after surgery, associated hemodynamic changes could lead to an acute drop in GFR[9]. Our data suggest that the mGFR did not change at 3 or 6 months postsurgery, suggesting an attenuation of the expected acute deterioration in kidney function (Table S1). Also, the observed correlations between leptin and mGFR suggest that leptin might act renoprotectively following surgery; further studies to understand this relationship and examine other potential mechanistic pathways are warranted.

Because measuring GFR is expensive and time-consuming, it is of interest whether novel filtration biomarkers can predict changes in mGFR in this setting. Given the loss of fat-free mass, serum creatinine and eGFR were expected to improve and did not correlate with mGFR. B2M is freely filtered, metabolized in the renal tubule, and reported to correlate with mGFR in other populations. Our results suggest its potential utility in bariatric surgery patients but its role as a biomarker of change in kidney function should be studied in other cohorts. In a recent study with mean mGFR 117±40 ml/min, cystatin C was associated with mGFR in those undergoing bariatric surgery[10]. However, we did not observe any changes in

cystatin C and such correlation. This may be attributed to the differences in baseline kidney function or to our study's small sample size.

In summary, bariatric surgery is associated with an improvement in insulin resistance, adipokines, and QoL, with no changes in kidney function at 12 months' follow-up. B2M correlates with mGFR in this setting. Cumulatively, this hypothesis-generating study argues for larger long-term studies in this area.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Changes in obesity, lipid, metabolic, kidney function, and QoL parameters before and 12 months after bariatric surgery

Variable	Baseline	12 months	Change	p
Obesity measures*				
Weight (kg)	160.3 [123.5, 172.0]	109.0 [96.1, 125.3]	−30.7 [−38.9, −24.0]	<0.001
Height (cm)	176.5 [172.0, 181.9]	--	--	
BMI (kg/m^2)	51.0 [36.8, 57.8]	34.4 [30.8, 46.7]	−9.3 [−14.0, −8.1]	<0.001
Waist circumference (cm)	138.5 [122.0, 157.5]	118.5 [106.0, 130.0]	−21.8 [−25.3, −15.0]	<0.001
Fat%	47.2 [40.1, 53.2]	34.2 [30.2, 44.6]	−10.2 [−15.7, −5.3]	<0.001
Fat mass (kg)	68.3 [46.0, 89.2]	37.4 [28.6, 59.8]	−24.8 [−31.5, −20.4]	<0.001
Fat-free mass (kg)	72.1 [68.5, 87.7]	68.4 [64.1, 77.6]	−7.6 [−10.1, −3.2]	0.002
Lipid parameters				
Total cholesterol (mg/dl)	134.0 [122.0, 146.0]	133.0 [107.0, 138.0]	−13.0 [−26.0, 15.0]	0.3
HDL cholesterol (mg/dl)	34.0 [31.0, 38.0]	44.0 [38.0, 61.0]	+11.0 [8.0, 14.0]	0.001
Serum triglycerides (mg/dl)	156.0 [106.0, 183.0]	99.0 [75.0, 119.0]	−54.0 [−90.0, 2.0]	0.05
LDL Cholesterol (mg/dl)	60.2 [47.6, 71.8]	57.4 [46.8, 69.2]	−0.80 [−23.0, 6.6]	0.5
Metabolic Parameters				
Log(hs-CRP)	0.98 [0.90, 1.00]	0.30 [−0.18, 0.76]	−0.56 [−1.1, −0.24]	<0.001
HOMA-IR	18.6 [5.2, 34.1]	4.8 [3.0, 6.0]	−13.8 [−29.2, −1.5]	0.008
Matsuda index	0.91 [0.42, 1.9]	2.4 [1.9, 2.7]	1.5 [0.51, 2.2]	0.04
HMW Adiponectin	2244 [1654, 3438]	6617 [2696, 7771]	1939 [869, 5559]	<0.001
Total Adiponectin	4815 [4339, 7858]	14491 [5837, 17756]	8329 [1021, 12180]	<0.001
Leptin	37.8 [22.8, 60.8]	10.6 [6.0, 16.1]	−15.7 [−26.2, −7.2]	0.001
Kidney function*				
Serum creatinine (mg/dl)	1.6 [1.5, 1.8]	1.4 [1.2, 1.6]	−0.27 [−0.34, −0.08]	0.006
Cystatin C (mg/dl)	1.8 [1.7, 1.9]	1.6 [1.5, 2.0]	0.02 [−0.17, 0.10]	0.5
B2M (mg/dl)	3.5 [3.3, 3.8]	3.5 [2.9, 3.8]	0.00 [−0.40, 0.40]	0.9
$eGFR_{cr}$ (ml/min)	47.7 [37.4, 52.4]	52.3 [45.1, 63.8]	7.9 [0.77, 16.2]	0.01
$eGFR_{cr}$ (ml/min/1.73 m^2)	30.5 [26.8, 34.5]	36.5 [35.9, 44.8]	11.0 [3.9, 14.3]	<0.001
$eGFR_{cys}$ (ml/min)	34.6 [33.4, 37.7]	41.7 [31.0, 46.2]	−0.73 [−2.5, 10.9]	0.3
$eGFR_{cys}$ (ml/min/1.73 m^2)	23.7 [22.4, 29.0]	28.9 [24.6, 34.9]	2.2 [0.57, 10.7]	0.003
$eGFR_{cr\text{-}cys}$ (ml/min)	41.6 [32.3, 47.2]	45.8 [34.6, 56.3]	4.8 [0.82, 9.2]	0.02
$eGFR_{cr\text{-}cys}$ (ml/min/1.73 m^2)	26.0 [25.2, 31.5]	34.3 [26.8, 41.9]	6.3 [3.4, 10.4]	<0.001
mGFR (ml/min)	82.0 [60.9, 89.7]	80.5 [63.0, 111.5]	1.2 [−1.6, 10.9]	0.3
mGFR (ml/min/1.73 m^2)	50.0 [44.0, 58.0]	64.0 [48.0, 87.0]	8.0 [5.0, 12.0]	0.02
24-h Proteinuria (g)	0.60 [0.16, 1.60]	0.43 [0.16, 0.85]	−0.02 [−0.28, 0.28]	0.8
QoL composite score				
SF-12 Physical Health	39.8[25.3,47.8]	49.1[42.1,51.6]	4.9[0.77,19.3]	0.007

Variable	Baseline	12 months	Change	p
SF-12 Mental Health	49.9[40.1,57.8]	56.4[48.9,58.2]	2.8[−1.6,11.6]	0.2

N = 13. Values are given as median [interquartile range].

*Wilcoxon signed rank test

Abbreviations: B2M, β_2-microglobulin; BMI, body mass index; cr, creatinine; cys, cystatin C; m/eGFR: measured/estimated glomerular filtration rate; HOMA-IR: homeostatic model assessment of insulin resistance; hs-CRP, high-sensitivity C-Reactive Protein; HMW, high-molecular-weight; SF-12, 12-Item Short Form Health Survey; HDL, high-density lipoprotein; LDL, low-density lipoprotein

Table 2

Spearman correlations between changes in kidney function parameters, obesity measures, adipokines, and insulin resistance

Variable	Correlation with change in	Rho (95% CI)	p
Change in mGFR (ml/min)	Matsuda index	0.33 (−0.30, 0.96)	0.3
	Leptin	−0.60 (−1.00, −0.07)	0.03
	Total adiponectin	0.08 (−0.58, 0.74)	0.8
	B2M	−0.65 (−1.00, −0.14)	0.02
	Cystatin C	−0.26 (−0.90, 0.38)	0.4
	Log(hs-CRP)	−0.50 (−1.00, 0.07)	0.08
Change in mGFR (ml/min/1.73 m^2)	Matsuda index	0.54 (−0.02, 1.00)	0.06
	Leptin	−0.74 (−1.00, −0.29)	0.004
	Total adiponectin	0.21 (−0.44, 0.86)	0.5
	B2M	−0.76 (−1.00, −0.33)	0.003
	Cystatin C	−0.36 (−0.98, 0.26)	0.2
	Log(hs-CRP)	−0.61 (−1.00, −0.09)	0.03
Change in Matsuda index	Leptin	−0.73 (−1.00, −0.28)	0.005
	Total adiponectin	0.24 (−0.41, 0.88)	0.4
	B2M	−0.47 (−1.00, 0.11)	0.1
	Cystatin C	−0.23 (−0.88, 0.41)	0.5
	Log(hs-CRP)	−0.35 (−0.97, 0.28)	0.3
Change in HOMA-IR	Leptin	0.63 (0.11, 1.00)	0.02
	Total adiponectin	−0.02 (−0.68, 0.65)	0.9
	B2M	0.76 (0.33, 1.00)	0.002
	Cystatin C	0.64 (0.13, 1.00)	0.02
	Log(hs-CRP)	0.12 (−0.54, 0.78)	0.7