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The effects of sleeve gastrectomy on renal function in diabetic and non-diabetic morbidly obese patients

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ABSTRACT

Introduction: Obesity is associated with albuminuria and impaired renal function. Bariatric surgery improves and resolves diabetes and restores renal function in patients with morbid obesity.
Objectives: This study investigates and compares the potential effects of sleeve gastrectomy on improving renal function and albuminuria in diabetic and non-diabetic morbidly obese patients.
Patients and Methods: This prospective study included 137 morbidly obese individuals (44 diabetics and 93 non-diabetic) who underwent laparoscopic sleeve gastrectomy. The patients were evaluated clinically (anthropometric measurements) and biochemically before surgery and at one year after surgery.
Results: Sleeve gastrectomy significantly decreased weight and body mass index (BMI), improves glycemic parameters, hyperfiltration, and urinary albumin excretion in diabetic and non-diabetic patients ($P<0.001$). Alterations in C-reactive protein (CRP) levels are strongly associated with albumin-to-creatinine ratio (ACR) decline in diabetic patients.
Conclusion: This study showed significant decreases in weight, BMI and glycemic parameters after sleeve gastrectomy in diabetic and non-diabetic individuals, accompanied by the resolution of hyperfiltration, urinary albumin excretion, and improvement of renal function by reduction of systemic inflammation.

Original

Implication for health policy/practice/research/medical education:
In a sleeve gastrectomy on 137 morbidly obese patients (44 diabetics and 93 non-diabetic), we found a significant decreases in weight, body mass index (BMI), and glycemic parameters after sleeve gastrectomy in diabetic and non-diabetic patients, accompanied by the resolution of hyperfiltration, urinary albumin excretion, and improvement of renal function by reduction of systemic inflammation. Therefore, sleeve gastrectomy would be beneficial in patients with diabetes and BMI greater than 35, restores and improves their renal function.

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Introduction

Obesity is a strong risk factor for the development of type 2 diabetes (T2DM), progression of chronic kidney disease, and end-stage renal disease (ESRD) (1,2).

Obesity independently impairs renal function by increasing the glomerular hyperfiltration, sodium handling in the proximal tubule, and sympathetic activation of the renin-angiotensin system (3).

In addition, insulin resistance and inflammation, resulting from adipose tissue-derived adipokines and the activated renin-angiotensin-aldosterone system (RAAS), are the main factors in unsustainable kidney hemodynamics and structure to decline kidney function (3).

Bariatric surgeries decrease obesity-associated inflammatory biomarkers and diseases such as diabetes, and improve obesity-related complications such as

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glomerular hyperfiltration and also proteinuria (4,5). Several studies have reported the benefits of weight loss on renal function and confirmed the positive effects of bariatric surgery on albuminuria, and proteinuria, including cohorts with either normal range, nephrotic range, or both (4-6).

Objectives

Regarding the effects of bariatric surgery on renal function, albuminuria, proteinuria, and impaired estimated glomerular filtration rate (eGFR), we investigate the results of bariatric surgery (sleeve gastrectomy) on renal function and albuminuria in obese diabetic and non-diabetic patients to find whether bariatric surgery could ameliorate albuminuria and reverse hyperfiltration.

Patients and Methods

Study design

This prospective study was carried out on patients referred to the endocrinology clinic of Loghman-Hakim hospital between 2017-2020 who were candidates for sleeve gastrectomy with BMI ≥40 kg/m² or BMI ≥35 kg/m² with underlying co-morbidities such as diabetes, cardiovascular disease, and sleep apnea (7).

Patients with a previous history of any bariatric surgery, macro-albuminuria (≥300 mg/g), severe chronic kidney disease (stage 3 or more), glomerulonephritis, hepatic failure, malignancy, inflammatory disease, or acute infectious disease were excluded.

Patients were divided into diabetic (DM) and non-diabetic (non-DM) groups. Patient data, including demographic information, body weight, height, waist circumference (WC), and systolic and diastolic blood pressure, were measured before and one year after surgery. Body mass index (BMI) is achieved by the division of weight (kg) by height (meters) squared.

Percentage total weight loss (%TWL) was calculated as [(preoperative weight − follow-up weight)/ (preoperative weight)] × 100.

In all patients, urine and serum samples were obtained preoperatively and 12 months after surgery to measure creatinine level, the eGFR, urinary albumin-to-creatinine ratio (UACR), fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), total cholesterol, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol, triglyceride, and high-sensitivity C-reactive protein (hs-CRP). eGFR (ml/min/1.73 m²) was calculated using the Cockroft-Gault formula, modified for obese patients using LBW (8). Hyperfiltration was defined as a GFR ≥125 mL/min/1.73 m² (9,10), albumin-to-creatinine ratio (ACR) ≥30-<300 mg/g was considered as abnormal(microalbuminuria), and resolution of albuminuria was defined as UACR, less than 30 mg/g were determined by a turbidometric test at the follow-up period.

The diagnosis of diabetes mellitus was according to the criteria established by the American Diabetes Association (ADA). These were fasting blood glucose ≥126 mg/dL or HbA1c ≥6.5 %. Diabetes remission was defined as FPG <126 mg/dL and HbA1c <6.5 %, in the absence of anti-diabetic medication (11). Remission of hypertension (HTN) was defined as blood pressure <140/90 mm Hg without antihypertensive medication.

Statistical analysis

Results are expressed as mean values and standard deviations of qualitative variables and absolute amount and percentage of quantitative variables. Paired *t* test and Wilcoxon signed-rank test were used to compare the groups (DM and non-DM) before and after the surgery. Chi-squared, independent sample *t* test, Fisher's exact test, Mann Whitney U test evaluate the effects of different factors on ACR improvement postoperatively in DM and non-DM groups. Independent predictive variables for albuminuria and regression of albuminuria after surgery were established with multivariable logistic regression analysis in all patients and DM groups.

All statistical analysis was conducted by the 23rd version of IBM SPSS statistical data analysis software.

Results

Table 1 shows baseline data of 137 patients categorized into diabetic (DM) and non-diabetic (non-DM) groups. Mean values and standard deviations of qualitative variables and absolute amount and percentage of quantitative variables are reported.

As demonstrated in Table 1, HTN is significantly more common among diabetic patients (61.4% versus 14% in DM and non-DM groups, respectively). Diabetes is also associated considerably with ACR ≥ 30 (P = 0.007). ACR ≥ 30 is detected in 40.9% of diabetic patients, while it was only detectable in 19.4% of non-diabetic patients.

Mean values of quantitative variables pre and post-operatively are compared in Table 2. As demonstrated in Table 2, a significant difference in BMI and WC amounts in diabetic and non-DM patients after the surgery was detected (P < 0.001). Following sleeve gastrectomy, we found significant decrease in systolic and diastolic blood pressure, FPG, HBA1c, and serum insulin levels in the DM group (P < 0.001).

Excellent glycemic control and HTN remission in 45% and 28.5% of diabetic patients turned into complete remission, while HTN remission in non- DM patients was 23% one year after surgery.

Bariatric surgery is also concomitant with reduced CRP levels in diabetic and non-DM patients after sleeve gastrectomy (P < 0.001).

Albumin-to-creatinine ratio and eGFR are both reduced in DM and non-DM patients after bariatric surgery, as shown in Figure 1.

Albumin-to-creatinine ratio ≥ 30 was detected in 40.9% of diabetic patients before interventions which declined to

Table 1. Clinical features of DM and non-DM groups at baseline

Variable	Diabetic group 44 (32.1%)	Non-Diabetic group 93 (67.9%)	*P* value
Age (years)	47.67 ± 8.57	37.69 ± 11.30	< 0.001*
Gender			
Male	8 (18.2%)	16 (17.2%)	0.8
Female	36 (81.8%)	77 (82.8%)	
Duration DM (y)	6.47 ± 5.47	0	
Weight (kg)	119.22 ± 25.25	122.15 ± 22.24	0.4
BMI (kg/m^2)	44.65 ± 6.18	46.98 ± 9.23	0.1
Waist circumference (cm)	125.45 ± 14.38	121.77 ± 18.95	0.2
HTN (yes/no)	27 (61.4%)/17(38.6%)	13 (14%)/80 (86%)	< 0.001*
Dyslipidemia (yes/no)	36 (81.8%)/8(18.2%)	60 (64.5%)/33 (35.5%)	0.03*
Mean ACR (mg/g)	39.74 ± 10.23	30.59 ± 14.26	0.1
ACR ≥ 30 mg/g (yes/no)	18 (40.9%)/26(59.1%)	18 (19.4%)/75(80.6%)	0.007*
Serum creatinine (mg/L)	0.94 ± 0.19	0.92 ± 0.13	0.5
GFR (mL/min/1.73 m^2)	131.52 ± 50.92	140.80 ± 51.04	0.1
FPG (mg/dL)	170.02 ± 57.82	99.20 ± 16.73	< 0.001*
HbA1c (%)	7.93 ± 1.47	5.47 ± 0.54	< 0.001*
Insulin Level (mg/dL)	24.54 ± 13.92	22.01 ± 13.18	0.6
CRP (mg/L)	8.54 ± 7.01	6.93 ± 6.46	0.1

DM: diabetes mellitus, BMI: body mass index, HTN: Hypertension, ACR: albumin-to-creatinine ratio, GFR: glomerular filtration rate, FPG: fasting plasma glucose, CRP: C- reactive protein.

Table 2. Clinical features of DM and non-DM groups before and one year after the surgery

Variable	Diabetic group			Non-diabetic group		
	Before	After	*P* value	Before	After	*P* value
BMI (kg/m^2)	44.65 ± 6.18	33.92 ± 4.78	<0.001*	47.21 ± 9.41	33.25 ± 7.65	<0.001*
TWL (%)		24.28 ± 6.43			27.60 ± 7.11	
WC (cm)	125.45 ± 14.38	108.93 ± 13.56	<0.001*	122.11 ± 19.65	102.21 ± 20.99	<0.001*
Systolic BP (mm Hg)	128.25 ± 15.42	116.62 ± 12.00	<0.001*	126.56 ± 18.43	110.57 ± 20.11	0.004*
Diastolic BP (mm Hg)	81.54 ± 15.25	74.74 ± 14.88	<0.001*	80.80 ± 16.78	74.45 ± 18.07	0.5
Serum Creatinine (mg/dL)	0.95 ± 0.18	0.89 ± 0.17	0.06	0.92 ± 0.13	0.99 ± 1.14	0.9
GFR (mL/min/1.73m^2)	131.52 ± 50.92	92.41 ± 30.53	<0.001*	140.80 ± 51.04	95.40 ± 32.90	<0.001*
Hyperfiltration (GFR> 125 mL/min/1.73 m^2)	20 (45.5%)	0 (0)		26 (56.5%)	7 (15.2%)	
ACR (mg/g)	39.74 ± 10.28	16.64 ± 11.66	<0.001*	30.59 ± 14.26	13.67 ± 13.79	<0.001*
ACR≥ 30 mg/g	18 (40.9%)	7 (15.9%)		18 (19.4%)	4 (4.3%)	
FPG (mg/dL)	170.02 ± 57.82	110.62 ± 26.10	<0.001*	99.26 ± 16.73	88.03 ± 13.21	<0.001*
HbA1c (%)	7.93 ± 1.47	6.34 ± 1.01	<0.001*	5.50 ± 0.52	5.32 ± 0.26	0.005*
Insulin level	23.61 ± 12.08	11.70 ± 4.90	<0.001*	22.27 ± 34.30	11.01 ± 5.54	0.06
CRP (mg/ L)	8.84 ± 7.10	3.40 ± 5.24	<0.001*	7.14 ± 6.42	3.28 ± 4.19	<0.001*
DM remission		20 (45%)				
HTN remission		7 (28.5%)			3 (23%)	

BMI, body mass index; TWL, total weight loss; WC, Waist circumference; BP, blood pressure; GFR, glomerular filtration rate; ACR, albumin-to-creatinine ratio; FPG, fasting plasma glucose; CRP, C-reactive protein; DM, diabetes mellitus; HTN, hypertension.

15.9% post-operatively (P < 0.001; 25% remission rate); Moreover, disappearances of hyperfiltration (eGFR> 120) achieved in 100% of diabetic patients and in 85% of non-diabetic patients.

We evaluated the effects of different factors on ACR improvement postoperatively in DM and non-DM groups, as noted in Table 3.

Our study showed a significant difference between CRP changes in groups with ACR < 30 and ACR ≥ 30 in diabetic patients (P = 0.04). It can be said that CRP changes are effective in improving postoperative albuminuria. As demonstrated in the above table, mean values of ACR baseline alterations were significantly lower in ACR < 30 groups (P = 0.001). Accordingly, no significant correlation between the variables mentioned above and ACR groups in non-diabetic patients was detected (P > 0.05).

Discussion

Our prospective observational study shows significant decreases in weight, BMI, glycemic parameters,

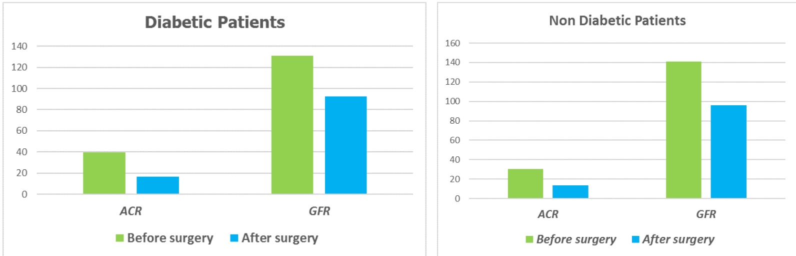

Figure 1. Mean values of ACR and eGFR in non- DM and DM group pre and postoperatively

normalization of hyperfiltration, and urinary albumin excretion after sleeve gastrectomy in diabetic and non-diabetic patients. Furthermore, our study suggests that sleeve gastrectomy can reduce albuminuria in diabetic patients with severe obesity by reducing systemic inflammation.

Similar to previous studies, we found obesity is associated with renal function changes, hyperfiltration, and microalbuminuria, independent of diabetes (4,5,12).

Obesity-related kidney damage, which has frequently been emphasized in the current literature is a condition with glomerular hyperfiltration, while the exact underlying pathophysiologic mechanisms are still unclear. Functional and structural renal abnormalities, including increased GFR and urinary albumin excretion, are seen in obese individuals (12).

Navarro-Diaz et al (6) noted that more significant proteinuria and albuminuria in severely obese patients than normal adults, since additional studies also provided this finding (4,5,12).

Glomerular hyperfiltration may occur in the earliest phase of nephropathy in cases with obesity or T2DM. Hyperfiltration and micro-albuminuria resolved in many patients following Roux-en-Y-gastric bypass and sleeve gastrectomy, suggesting bariatric surgery can reverse early renal functional changes associated with morbid obesity (13,14).

Our study confirms previous studies that concluded bariatric surgeries could improve renal function in obese patients. Reid et al evaluated changes in renal function, ACR, and GFR in a larger cohort of patients, undergoing Roux-en-Y gastric bypass or sleeve gastrectomy. One year after the surgery, micro-albuminuria resolved in most of the patients, and hyperfiltration was also decreased in nearly half of them, which was a dedicated improvement of renal function (14).

The effects of weight loss on the absolute amount of GFR and hyperfiltration are controversial. This challenge can be attributed to different equations to measure GFR. Similar to our study, Serra et al showed that bariatric surgery significantly improves albuminuria and creatinine clearance in highly obese patients within the first year of surgery (15).

It is noteworthy to imply the study of Kim et al, who reported an improvement in micro-albuminuria and renal function within the first year after surgery. However in their study, the improvement of eGFR was not significant (16). Nevertheless, using two different bariatric surgery techniques can affect the final results of the study by Kim et al as other techniques of bariatric surgery have different outcomes (16,17).

Likewise, Young et al by long-term follow-up of 101

Table 3. Evaluation of the effects of different factors on ACR improvement in DM and non-DM groups

Variable	Diabetic group			Non-diabetic group		
	ACR < 30	ACR ≥ 30	*P* value	ACR < 30	ACR ≥ 30	*P* value
TWL (%)	24.55 ± 6.16	22.87 ± 8.11	0.5	27.83 ± 7.08	22.81 ± 6.75	0.1
Δ BMI	10.91 ± 3.66	9.79 ± 4.46	0.4	14.11 ± 7.39	10.72 ± 3.71	0.3
Δ SBP	11.47 ± 11.24	12.50 ± 14.74	0.8	15.42 ± 22.16	33.50 ± 23.33	0.2
Δ DBP	7.42 ± 10.52	8.33 ± 10.80	0.8	6.30 ± 25.94	7.50 ± 10.60	0.9
Δ FPG	63.58 ± 49.44	37.28 ± 51.39	0.2	11.42 ± 16.74	5.75 ± 3.30	0.5
Δ HbA1c	1.70 ± 1.10	0.92 ± 1.58	0.1	0.17 ± 0.51	0.15 ± 0.41	0.9
Duration of DM	6.29 ± 5.74	7.42 ± 3.86	0.6			
Δ Insulin level	12.44 ± 8.85	6.72 ± 6.81	0.08	11.32 ± 4.40	10.01 ± 6.55	0.9
Δ CRP	6.19 ± 5.02	1 ± 0.45	0.041	4.09 ± 3.1	0.62 ± 0.12	0.2
Δ WC	16.35 ± 8.94	17.42 ± 13.97	0.8	19.02 ± 19.71	37.35 ± 52.46	0.5
Δ GFR	43.01 ± 29.55	19.60 ± 34.22	0.06	44.55 ± 28.32	17.47 ± 11.10	0.06
Δ Serum creatinine	0.08 ± 0.15	- 0.08 ± 0.23	0.02*	0.66 ± 0.18	0.1 ± 0.08	0.9
ACR baseline	33.28 ± 22.53	78.50 ± 43.14	< 0.001*	25.43 ± 25.99	95.75 ± 71.40	0.1

BMI, body mass index; TWL, total weight loss; WC, Waist circumference; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; GFR, glomerular filtration rate; ACR, albumin-to-creatinine ratio; FPG, fasting plasma glucose; CRP, C-reactive protein; DM, diabetes mellitus.

diabetic patients with albuminuria who underwent bariatric surgery, showed a significant improvement in albuminuria post-operatively in 80% of their patients (18). On the other hand, Adam et al demonstrated that the improvement in glomerular hyperfiltration in obese people with T2DM, is not accompanied by any change in ACR within 12 months after surgery (19).

Elbasan et al highlighted notable decreases in weight, BMI, and glycemic indices following sleeve gastrectomy in diabetic and non-diabetic patients, which was not accompanied by no significant alteration in micro-albuminuria (20), which might be related to the short duration of follow-up and small sample size.

The change in BMI from baseline within the 12 months post-operative is not a significant predictor of ACR normalization on logistic regression analysis. A similar observation was reported in a series of non-diabetic morbid obesity subjects undergoing bariatric surgery (3,4,6).

Magalhães et al reported that the urinary albumin creatinine ratio notably decreases after weight loss following bariatric surgery. They showed BMI, systolic blood pressure and HbA1c significantly predict urinary albumin excretion (21).

Similar to our study, Navaneethan et al failed to find any association between weight loss and ACR normalization. They however reported an association between the surgical technique and ACR normalization (22).

Amor et al conducted a study with a significant study population of diabetic patients who underwent bariatric surgery (Roux-en-Y gastric bypass (n = 255), sleeve gastrectomy (n = 96)). They showed that weight loss independently predicts urinary albumin excretion normalization in morbidly obese type 2 diabetic patients undergoing bariatric surgery (23), confirmed by another study (7).

We should highlight that in our study, the reduction of CRP levels is the most critical factor affecting the reduction of albuminuria in diabetic patients after the surgery; neither the rate of weight loss nor the improvement of the glycemic index was as much as effective as CRP reduction. Previous studies have shown that in diabetic patients with albuminuria, CRP levels are high. Improved systemic inflammation after bariatric surgery is accompanied by decreased albuminuria and reversing diabetes nephropathy (24). Chronic inflammation is one of the essential pathologic processes affecting renal function in obese diabetic patients, since weight loss achieved by bariatric surgeries ameliorates this condition (25).

Finally, the improvement of renal function after bariatric surgery is a multifactorial process resulting from the progress of glomerular hyperfiltration, better glycemic control, decreased peripheral insulin resistance, and amelioration of inflammatory cytokines. Our results are in consist with this theory.

Conclusion

This study provides sleeve gastrectomy as a treatment of choice in patients with underlying renal abnormality, which significantly reduces systemic blood pressure, BMI, glycemic parameters, resolve the hyperfiltration and urinary albumin excretion; and improves renal function by lowering systemic inflammation.

Limitations of the study

Our study also has some limitations; we only studied obese patients who underwent sleeve gastrectomy, while patients who received medical treatment for obesity or underwent other bariatric surgery techniques are not included in our study. The relatively small population and short follow-up period are other limitations. We propose further studies with lager sample size, more extended follow-up periods, and include other medical or bariatric surgical techniques.

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Authors' contribution

ZD, NZ, SST, MS, and SHM conducted the research. ZD, SHM, and YF finalized the manuscript. All authors read and signed the final manuscript.

Conflicts of interest

At this moment, it is declared that we do not have any conflicts of interest.

Ethical issues

We received approval of the research proposal through the research committee of the internal medicine department of the Loghman-Hakim hospital affiliated with the Shahid Beheshti University of Medical science, Tehran (Iran). At each research stage, we followed the considerations of the Declaration of Helsinki and the Ethics Committee of the Ministry of Health. Each participant signed the informed written consent form. This project was also confirmed by the Ethics Committee of the Shahid Beheshti University of Medical Sciences (#IR. SBMU.MSP.REC.1398.503). This study was extracted from the Sahab-Sadat Tabatabaei residential thesis in the department of internal medicine.

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