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ORIGINAL CONTRIBUTIONS

The Relationship Between Preoperative Kidney Function and Weight Loss After Bariatric Surgery in Patients with Estimated Glomerular Filtration Rate ≥ 30 mL/min: Tehran Obesity Treatment Study

Maryam Barzin[1] · Pouria Mousapour[1] · Alireza Khalaj[2] · Maryam Mahdavi[1] · Majid Valizadeh[1] · Farhad Hosseinpanah[1]

Abstract

Introduction Severe obesity can lead to progressive kidney injury and chronic kidney disease (CKD). The current study aimed at determining whether preoperative kidney function level in patients with estimated glomerular filtration rate (eGFR) ≥30 mL/min affects weight loss after bariatric surgery.

Methods A total of 1958 bariatric patients underwent laparoscopic sleeve gastrectomy and gastric bypass from March 2013 to March 2017. The patients were categorized according to preoperative eGFR (30–59, 60–89, 90–124, and ≥ 125 mL/min). Changes in body mass index (BMI), percentage of total weight loss (TWL%), and percentage of excess weight loss (EWL%) were compared across the eGFR categories. Moreover, multivariable logistic regression analysis was used to evaluate the relationship between eGFR and insufficient weight loss (defined as not achieving 50% EWL at 12 months after surgery).

Results Preoperative eGFR was positively associated with unadjusted ΔBMI (*P* trend < 0.001), TWL% (*P* trend < 0.001), and EWL% (*P* trend = 0.007) after 12 months of surgery. However, these associations were no longer significant after multivariable adjustment. Further, univariate analysis demonstrated a positive relationship between preoperative eGFR and insufficient weight loss (odds ratio [OR] 1.38; 95% confidence interval [CI] 1.11–1.71; *P* = 0.004). By contrast, preoperative eGFR was not a predictor of insufficient weight loss in multivariable logistic regression analysis (OR 0.98; 95% CI 0.46–1.24; *P* = 0.886).

Conclusion Although patients with lower preoperative eGFR experience less weight loss after bariatric surgery, preoperative kidney function does not appear to have an independent impact on postoperative weight loss in patients with eGFR ≥ 30 mL/min.

Keywords Bariatric surgery · Kidney function · Glomerular filtration rate · Weight loss

Introduction

Severe obesity (body mass index [BMI] ≥ 35 kg/m^2) is an enormous global health challenge, with an exponentially increased global prevalence over the past several decades [1]. Obesity is recognized as a complex disease state due to its association with several chronic conditions including dyslipidemia, hypertension, low-grade systemic inflammation, insulin resistance and diabetes, and cardiovascular damage [2]. It is also regarded as a central risk factor for the onset and progression of chronic kidney disease (CKD) [3, 4].

Bariatric surgery is established as the only intervention to provide a sustained treatment of severe obesity and its related comorbidities [5]. The number of patients undergoing bariatric surgery has increased globally, parallel to the increasing demand and accessibility, as well as advances in laparoscopic surgery. Laparoscopic gastric bypass (LGB) and laparoscopic sleeve gastrectomy (LSG) are the two most effective and thus most preferred bariatric procedures [6], leading to, respectively, 63–72% and 51–70% excess weight loss (EWL) after 1 year [7]. Despite these promising results, up to 15% of patients do not experience sufficient weight loss after the surgery. To date, a multitude of demographic and surgical factors such as patient's age, gender, preoperative BMI, obesity-

✉ Farhad Hosseinpanah
fhospanah@endocrine.ac.ir

1 Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 Tehran Obesity Treatment Center, Department of Surgery, Faculty of Medicine, Shahed University, Tehran, Iran

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related comorbidities, type of surgical procedure, postoperative exercise, and dietary restraint have been suggested to be independently related to insufficient weight loss post-bariatric surgery [8–11].

Severe obesity can lead to progressive kidney injury and CKD. Not only comorbidities of obesity but obesity per se also results in a spectrum of renal injuries and the development of CKD through regulation of a deleterious inflammatory profile, regulation of oxidative stress, and alterations in kidney hemodynamics [4, 12]. Due to the progressive nature of CKD and irreversibility of kidney function in more severe stages of the disease [13], estimating the timing of bariatric surgery in patients with CKD raised the attention of researchers in recent years. The stage of CKD before bariatric surgery have been previously shown to be independently associated with increasing risk for 30-day incidence of postoperative surgical site complications, various infectious diseases, cardiovascular events, and clotting disorders [14, 15]. Moreover, a recent study indicated eGFR < 30 mL/min as an independent factor for attenuated weight loss [16]. Nonetheless, there is no evidence on the efficacy of bariatric surgery in patients with eGFR ≥ 30 mL/min.

The current study primarily investigated whether preoperative kidney function in patients with eGFR ≥ 30 mL/min is associated with attenuated weight loss at 6 and 12 months after bariatric surgery. The study also examined whether preoperative eGFR is an independent predictive factor of insufficient weight loss 12 months after surgery.

Materials and Methods

Study Design and Participants

The current prospective study was conducted within the framework of Tehran Obesity Treatment Study (TOTS), the single-institution cohort of patients with excessive obesity, which introduces patients who are candidates for bariatric surgery to our referral bariatric center in three university hospitals in Tehran, Iran. A detailed description of the TOTS is provided elsewhere [17]. The study population was initially consisted of 4037 patients, aged 18 to 65 years receiving either LGB (one-anastomosis gastric bypass and Roux-en-Y gastric bypass) or LSG from March 2013 to March 2017, due to BMI of > 40 or > 35 kg/m^2 in the presence of at least one obesity-related comorbidity (diabetes mellitus, hypertension, and dyslipidemia). Then, the ones with preoperative eGFR < 30 mL/min, those undergoing revision surgery, and patients with insufficient follow-up information were excluded, leaving 1958 eligible subjects for the analysis.

All surgeries were performed by the same team of experienced surgeons. Demographic characteristics including age, gender, and medical and drug histories were recorded pre- and post-operatively during scheduled follow-up visits according to the study protocol [17].

Definitions

Type 2 diabetes mellitus (T2DM) was defined according to the American Diabetes Association as glycated hemoglobin (HbA1c) ≥ 6.5%, fasting plasma glucose ≥ 126 mg/dL, or use of antidiabetic medication [18]. Hypertension was defined as a systolic blood pressure of ≥ 140 mmHg, a diastolic blood pressure of ≥ 90 mmHg, previous diagnosis of hypertension, or use of antihypertensive medication [19]. Dyslipidemia was defined as serum triglycerides (TG) ≥ 200 mg/dL, total cholesterol (TC) ≥ 240 mg/dL, low-density lipoprotein (LDL) ≥ 160 mg/dL, high-density lipoprotein < 40 mg/dL, or receiving lipid-lowering therapy [20].

Body surface area (BSA; m^2) was calculated for each individual using the DuBois & DuBois formula as 0.007184 × height (cm)$^{0.725}$ × weight (kg)$^{0.425}$ [21]. Serum creatinine (cr) levels were assayed using the Jaffe kinetic method. Preoperative GFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [22], multiplied by BSA/1.73 m^2 and categorized as follows: 30–59, 60–89, 90–124, and ≥ 125 mL/min.

Weight reduction for each patient at 6 and 12 months after surgery was expressed as change in BMI (ΔBMI), percentage of total weight loss (TWL%), and percentage of excess weight loss (EWL%) as follows:

- ΔBMI = postoperative BMI − preoperative BMI
- TWL% = (preoperative weight − postoperative weight)   preoperative weight × 100
- EWL% = (preoperative weight − postoperative weight)   (preoperative weight − weight corresponding to BMI at 25 kg/m^2) × 100

Insufficient weight loss was defined according to the Reinhold criteria as not achieving 50% EWL at 12 months after surgery [23].

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation and categorical data as frequency and percentages. Clinical characteristics of the study patients were compared across the eGFR categories using one-way analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. ANOVA was also used for unadjusted comparison of ΔBMI, TWL%, and EWL% across the preoperative eGFR categories. Moreover, a one-way analysis of covariance (ANCOVA) was used for comparisons across the categories with adjustment for potential confounders including age, gender, preoperative BMI, procedure type,

Table 1 Clinical characteristics of the study patients across preoperative eGFR categories

	Total ($n = 1958$)	eGFR (mL/min)				P value
		≥ 125 ($n = 647$)	90–124 ($n = 883$)	60–89 ($n = 406$)	30–59 ($n = 22$)	
Females, *n* (%)	1566 (80.0)	365 (56.4)	790 (89.5)	392 (96.6)	19 (86.4)	< 0.001
Age (years)	38.82 ± 11.03	32.46 ± 8.27	39.10 ± 9.94	47.41 ± 10.33	56.00 ± 7.02	< 0.001
Weight (kg)	121.10 ± 20.65	133.10 ± 22.70	117.55 ± 16.88	110.32 ± 15.21	109.76 ± 11.69	< 0.001
BMI (kg/m^2)	45.07 ± 5.99	46.38 ± 6.22	44.69 ± 5.86	43.84 ± 5.52	44.19 ± 6.16	< 0.001
BSA (m^2)	2.22 ± 0.23	2.36 ± 0.25	2.18 ± 0.18	2.08 ± 0.16	2.08 ± 0.16	< 0.001
Hypertension, *n* (%)	598 (32.2)	150 (24.8)	270 (32.1)	164 (42.1)	14 (66.7)	< 0.001
T2DM, *n* (%)	540 (28.6)	126 (20.7)	240 (27.9)	161 (40.6)	13 (61.9)	< 0.001
Dyslipidemia, *n* (%)	1032 (53.8)	318 (51.5)	457 (52.3)	241 (59.5)	16 (72.7)	0.015
Procedure type (LSG/LGB), %	63.5/36.5	66.6/33.4	61.3/38.7	64.0/36.0	54.5/45.5	0.144
Serum creatinine (mg/dL)	0.90 ± 0.17	0.81 ± 0.16	0.89 ± 0.12	1.03 ± 0.13	1.42 ± 0.35	< 0.001
eGFR (mL/min)	114.30 ± 30.20	148.45 ± 21.32	106.90 ± 9.77	79.29 ± 7.65	53.21 ± 5.25	< 0.001

Values are presented as frequency (percentages) or mean ± standard deviation

eGFR, estimated glomerular filtration rate; *BSA*, body surface area; *T2DM*, type 2 diabetes mellitus; *LSG*, laparoscopic sleeve gastrectomy; *LGB*, laparoscopic gastric bypass

T2DM, hypertension, and dyslipidemia. Multivariable logistic regression analysis was used to test the relationship between a change in the preoperative eGFR categories and insufficient weight loss. The analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA), and P value < 0.05 was considered statistically significant.

Results

Baseline characteristics of the study patients are outlined in Table 1. Of the total 1958 patients (80.0% female) included in the study, 647 (33%) had eGFR ≥ 125, 883 (45.1%) had eGFR 90–124 mL/min, 406 (20.7%) had eGFR 60–89 mL/min, and 22 (1.1%) had eGFR 30–59 mL/min. The category of preoperative eGFR ≥ 125 mL/min comprised the youngest group of patients, and mean age increased across the eGFR categories. The prevalence of obesity-related comorbidities was higher in patients with lower preoperative eGFR. There was no significant difference regarding the proportion of procedure types between the preoperative eGFR categories.

Over 6 months after bariatric surgery, slower weight loss was observed in patients with preoperative eGFR 30–59 and 60–89 mL/min, compared with those with preoperative eGFR 90–124 and ≥ 125 mL/min as well as in patients with preoperative eGFR 90–124 mL/min, compared with those with preoperative eGFR ≥ 125 mL/min. Over the second 6-month period, patients with preoperative eGFR 30–59 mL/min did not present significant weight loss, and the slope of weight loss decreased with more reduced preoperative eGFR values across all study groups (Fig. 1).

Weight loss measures during 6 and 12 months after bariatric surgery were assessed and compared across the preoperative eGFR categories. As demonstrated in Table 2, significant trends of decreasing ΔBMI and TWL% after 6 and 12 months and EWL% after 12 months were observed in an unadjusted

Fig. 1 Trends in weight loss during 12 months after bariatric surgery across different preoperative eGFR groups

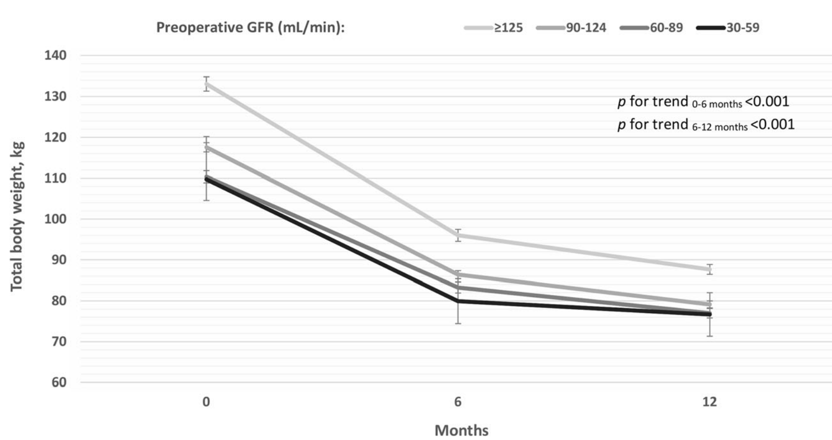

Table 2 Weight loss results 6 and 12 months after bariatric surgery across preoperative eGFR categories

		eGFR (mL/min)				*P* for ANOVA
		≥ 125	90–125	60–90	30–60	
Unadjusted	6 months post-op					
	ΔBMI (kg/m^2) (SE)	− 12.97 (0.11)	− 11.87 (0.09)	− 11.02 (0.13)	− 10.52 (0.53)	< 0.001
	%TWL (SE)	27.81 (0.19)	26.47 (0.16)	24.95 (0.24)	24.70 (1.01)	< 0.001
	%EWL (SE)	62.52 (0.56)	62.65 (0.50)	60.71 (0.81)	63.43 (3.27)	0.162
	12 months post-op					
	ΔBMI (kg/m^2) (SE)	− 15.79 (0.17)	− 14.61 (0.14)	− 13.21 (0.19)	− 13.48 (0.81)	< 0.001
	%TWL (SE)	33.84 (0.28)	32.49 (0.24)	30.04 (0.35)	30.27 (1.40)	< 0.001
	%EWL (SE)	76.25 (0.71)	76.80 (0.64)	73.01 (0.99)	73.46 (3.78)	0.007
Adjusted*						*P* for ANCOVA
	6 months post-op					
	ΔBMI (kg/m^2) (SE)	− 12.28 (0.10)	− 12.34 (0.10)	− 12.30 (0.14)	− 12.68 (0.52)	0.861
	%TWL (SE)	26.99 (0.23)	27.13 (0.21)	26.91 (0.30)	27.77 (1.15)	0.780
	%EWL (SE)	62.79 (0.57)	63.24 (0.53)	63.19 (0.77)	65.73 (2.88)	0.237
	12 months post-op					
	ΔBMI (kg/m^2) (SE)	− 14.74 (0.15)	− 15.06 (0.14)	− 14.81 (0.20)	− 15.64 (0.70)	0.191
	%TWL (SE)	32.32 (0.32)	33.02 (0.31)	32.43 (0.44)	34.26 (1.52)	0.170
	%EWL (SE)	74.93 (0.77)	76.38 (0.73)	75.30 (1.05)	80.06 (3.60)	0.762

SE, standard error; *BMI*, body mass index; *TWL*, total weight loss; *EWL*, excess weight loss; *eGFR*, estimated glomerular filtration rate

*Adjusted for age, sex, type 2 diabetes mellitus, hypertension, dyslipidemia, procedure type, and initial BMI

analysis, corresponding to decreasing GFR. These trends, however, turned out to be insignificant after multivariable adjustment.

Insufficient weight loss was observed in 39 (6.0%) patients with preoperative eGFR ≥ 125 mL/min; 62 (7.0%) patients with preoperative eGFR 90–124 mL/min, 46 (11.3%) patients with preoperative eGFR 60–89 mL/min, and two (9.1%) patients with preoperative eGFR 30–59 mL/min. In a univariate analysis, older age, female gender, higher initial BMI, LSG, T2DM, hypertension, and dyslipidemia were significantly associated with insufficient weight loss 12 months after bariatric surgery. Moreover, increasing risk of insufficient weight loss was observed per each change in the preoperative eGFR categories (OR 1.38; 95% CI 1.11–1.71; $P = 0.004$). In a multivariable logistic regression analysis, preoperative eGFR, per each change in the categories, was not independently associated with insufficient weight loss. Independent predictors for insufficient weight loss included older age, female gender, higher initial BMI, LSG, and dyslipidemia (Table 3).

Discussion

To the best of our knowledge, it was the first prospective study to date exploring the impact of preoperative eGFR on weight loss following bariatric surgery. In the current study among patients with eGFR ≥ 30 mL/min, despite an actual association between preoperative eGFR and weight loss response to bariatric surgery, decreased eGFR did not remain an independent predictor of insufficient post-bariatric weight loss after adjustment for potential confounders and other predictors.

These findings are in agreement with a retrospective multicenter study in France on 101 patients categorized according to their preoperative eGFR as < 30, 30–59, 60–89, and ≥ 90 mL/min/1.73 m^2 [16]. In spite of increasing trends of EWL and TWL after 6 and 12 months of bariatric surgery across, these significant trends were no longer observed in a sub-analysis of patients with eGFR ≥ 30 mL/min/1.73 m^2, after adjustment for confounders including age, gender, initial BMI, type of procedure (LSG/LGB), and T2DM [16], meaning that in this population of patients, a lower preoperative eGFR per se had no impact on weight loss after bariatric surgery.

The etiology of insufficient weight loss after bariatric surgery is multifactorial, and the previously suggested influencing factors are considerably overlapping. In the current study, although weight loss after bariatric surgery was more attenuated in patients with lower preoperative eGFR levels, other factors including older age, female gender, dyslipidemia, and higher initial BMI and LSG were the independent predictors of insufficient weight loss. Thus, it can be pointed out that in this cohort of patients with eGFR ≥ 30 mL/min, insufficient weight loss could have potentially been driven by factors other

Table 3 Association of patients characteristics with insufficient weight loss (1-year excess weight loss < 50%)

		Univariate analysis		Multivariable logistic regression analysis	
Variables	Insufficient weight loss (%)	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age		1.04 (1.03–1.06)	< 0.001	1.03 (1.01–1.05)	0.005
Sex					
Male	3.8	Reference			
Female	8.6	2.35 (1.36–4.06)	0.002	2.24 (1.28–4.46)	0.010
T2DM					
No	6.5	Reference			
Yes	10.9	1.76 (1.24–2.48)	0.001	1.26 (0.83–1.89)	0.274
Hypertension					
No	6.1	Reference			
Yes	10.4	1.77 (1.25–2.52)	0.001	1.02 (0.68–1.57)	0.922
Dyslipidemia					
No	6.3	Reference			
Yes	8.9	1.45 (1.03–2.05)	0.035	1.49 (1.01–2.22)	0.046
Procedure type					
LGB	5.6	Reference			
LSG	8.8	1.62 (1.11–2.35)	0.012	2.31 (1.52–3.51)	< 0.001
Initial BMI		1.10 (1.07–1.13)	< 0.001	1.10 (1.07–1.13)	< 0.001
Preoperative eGFR		1.38 (1.11–1.71)	0.004	0.98 (0.46–1.24)	0.886

T2DM, type 2 diabetes mellitus; *LGB*, laparoscopic gastric bypass; *LSG*, laparoscopic sleeve gastrectomy; *BMI*, body mass index; *eGFR*, estimated glomerular filtration rate; *OR*, odds ratio; *CI*, confidence intervals

than a decreased preoperative eGFR. Likewise, in line with most previous studies, the current study indicated aging and coexistence of dyslipidemia as risk factors for less weight loss after bariatric surgery [24, 25]. This reflects that weight loss in more decreased preoperative eGFR categories could be, at least in part, induced by older age and higher proportion of dyslipidemia in such patients. In contrast with the literature, however, we observed no independent association between T2DM and weight loss in the current cohort [11, 25]. Meta-analyses also support more enhanced weight loss after performing LGB compared with LSG [26, 27]. In this regard, although in our study, LGB was independently associated with insufficient weight loss after 1 year of surgery, our study groups were comparable for the proportion of procedure types. Taken together, it seems that the impact of preoperative eGFR on weight loss response to bariatric surgery is independent of the type of procedure. Finally, our findings regarding the impact of gender on post-bariatric weight loss were in contrast with those of previous studies reporting either gender as ineffective or male gender as a predictor of lower post-bariatric weight loss [9, 11, 28].

There is also limited evidence on efficacy of bariatric surgery in terms of resolution of comorbidities as well as incidence of postoperative complications in patients according to their preoperative kidney function level. A 12-month follow-up of 233 patients with eGFR ≥ 30 mL/min in China showed significantly lower reduction of TG, TC, LDL, systolic blood pressure, and HbA1c as well as lower remission of T2DM after bariatric surgery in patients with preoperative eGFR 30–59 mL/min compared with those with higher preoperative eGFR values. In the mentioned study, Hou et al. however reported similar TWL% and ΔBMI after 12 months of bariatric surgery across preoperative eGFR categories [29]. Moreover, in a retrospective study using the US national metabolic and bariatric surgery database, patients with serum Cr > 2 mg/dL but not requiring hemodialysis were at higher risk for 30-day complications of bariatric surgery [15]. Likewise, in the study by Turgeon et al., 30-day complications of bariatric surgery were independently associated with decreasing preoperative eGFR across the categories of ≥ 90, 60–89, 30–59, and < 30 mL/min/1.73 m^2 [14].

The current study was the first prospective study that compared the efficacy of bariatric surgery across different preoperative eGFR categories and evaluated the independent association between preoperative eGFR and insufficient weight loss following bariatric surgery within the framework of a well-defined continuous cohort. However, the current study had important limitations to consider. We did not have data on proteinuria, and thus, analyses could not be performed according to the CKD stages defined by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines [30]. Moreover, absolute GFR was estimated using the CKD-EPI formula rather than its directly measured values using a gold standard method. Although the CKD-EPI formula is the most accurate Cr-based method to estimate GFR in severe obesity [31], BSA normalization removal further mitigates the bias imposed by an extreme BSA and leads to the highest concordance with measured eGFR values [31, 32]. A small sample size of patients with preoperative eGFR of 30–60 mL/min was utilized in the present study; thus, the findings regarding the potential impact of preoperative eGFR in this category should be interpreted with caution.

Conclusion

Although patients with lower preoperative eGFR may experience less weight loss after bariatric surgery, preoperative eGFR does not appear to have an independent impact on postoperative weight loss among patients with eGFR ≥ 30 mL/min. Further studies with larger sample sizes of patients with more impaired kidney function, and by integration of eGFR and albuminuria, are needed to verify our findings and to explore the most effective, durable, and the safest bariatric option for patients in different CKD stages.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional Human Research Review Committee (No. 2ECRIES 93/03/13) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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