## **ORIGINAL CONTRIBUTIONS**





# Improvement of Renal Function After Bariatric Surgery: a Systematic Review and Meta-analysis

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#### Abstract

**Background/Objective** The effect of bariatric surgery in renal function varies and the postoperative benefit time point remains unclear. We aim to assess the changes of renal function after bariatric surgery (BS) in different postoperative periods and subgroups. **Methods** We searched the databases of PubMed and Cochrane from inception to December 14, 2020. Articles included in the study were drawn from all recipients of BS that provided assessments of renal function pre and post-surgery. Meta-analysis was performed to compare glomerular filtration rate (GFR), serum creatinine, albumin-to-creatinine ratio (ACR), and albuminuria before and after BS.

**Results** The study included 49 articles involving 8515 patients. Compared with pre-operative renal function, the overall analysis showed that bariatric surgery significantly reduced serum creatinine levels, ACR, and albuminuria. There was significant increase of GFR in the CKD subgroup, yet a noticeable decrease in the hyperfiltration subgroup. The most significant improvement in GFR was seen 6–12 months after BS, while ACR dropped most dramatically 12–24 months after BS. **Conclusions** Bariatric surgery can improve renal function in obese patients with kidney dysfunction, especially 1 year after surgery.

**Keywords** Bariatric surgery · Renal function · Obesity · Meta-analysis

# Introduction

Obesity is a serious risk factor for the occurrence and development of chronic kidney disease (CKD). Obesity not only indirectly increases the risk of CKD through diabetes and

#### **Key Points**

• Bariatric surgery can improve renal function only in obese patients with kidney dysfunction.

Renal function improved most after 1 year of bariatric surgery.
Compared with RYGB (Roux-en-Y gastric bypass), patients received SG (sleeve gastrectomy) benefited more in the reduction of serum creatinine.

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hypertension, but also directly affects renal function and structure [1]. The high filtration rate caused by obesity gradually decreased, along with the development of obesity-related renal damaged, and eventually developed into end-stage renal disease [2]. In the setting of obesity, the main clinical manifestations of kidney disease were proteinuria, albuminuria, hyperfiltration, or decreased glomerular filtration rate [3].

Bariatric surgery is one of the most effective treatments to maintain long-term weight loss. The obesity-related complications are significantly improved after BS such as

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hypertension, dyslipidemia, and diabetic complications and and [4–6]. The improvement of these complications will have a positive effect on the kidney theoretically. Several previous studies have also showed that BS can improve renal function [7–9]. However, in other studies, BS is regarded as a risk factor to acute kidney damage and is associated with hyperoxaluria which can lead to kidney stone formation and renal insufficiency [10, 11]. Therefore, the effect of bariatric surgery on renal function remains controversial.

There are some previous meta-analysis of the effect of BS on renal function. However, these studies were limited to the analysis of single renal function indicators or specific patients such as patients with T2D or CKD [12–14]. Moreover, these meta-reviews did not compare the impact of bariatric surgery on renal function between different BS methods or different follow-up stages. Several important studies with larger sample size were reported recently regarding the changes in pre- and post-operative renal function, which may provide further evidence for the influence of BS on renal function [9, 15–18]. Therefore, we included the latest relevant literature and more evaluation index of renal function to conduct a more comprehensive meta-analysis of the influence of BS on renal function.

## **Materials and Methods**

#### Search Strategy

Two authors independently searched published studies indexed in the databases of PubMed and Cochrane from inception to December 14, 2020. The search keywords are as follows: bariatric surgery, metabolic surgery, gastric bypass, gastric banding, Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), renal function, renal outcomes, glomerular filtration rate, serum creatinine, creatinine clearance, albuminuria, 24-h urine albumin excretion rate, and urine albumin-to-creatinine ratio.

## **Study Selection**

We screened all the articles that participants received bariatric surgery and reported renal function indexes before and after surgery. The renal function indexes included GFR, serum creatinine, albuminuria, and ACR. The bariatric surgery mainly included RYGB and SG, but not limited to these two types of surgery. The patients did not have specific limits if the participants met the bariatric surgical indications. Reviews, case reports, or meta-analysis was excluded. Articles that had no follow-up rate, no available data, or based on the same study population were excluded.

#### **Data Extraction and Synthesis**

This review included all published randomized controlled trials or observational studies that assessed the change of GFR, serum creatinine, albuminuria, and ACR after BS. The pre- and post-surgery mean values with standard deviation (or standard error) of those renal function indexes were collected and included in the analysis. The continuous data provided in some studies were median and interquartile ranges, which were inconsistent with other articles, so they were not included in the analysis. For articles that reported renal function indexes at multiple follow-up time, we selected the data of the longest follow-up to analysis; only in subgroup analysis based on different follow-up periods after bariatric surgery, we included the date of all follow-up time reported in the article. The information of study design, baseline clinical characteristics of the study population, type of surgery, and duration of follow-up were extracted in all included articles.

#### **Quality Assessment**

Two authors assessed the study quality for all included observational studies using the Newcastle–Ottawa scale (NOS). A total score of 3 or less was considered poor quality. We excluded studies from our meta-analysis if they had poor quality. Discrepant opinions were resolved by consultation between all authors.

#### **Statistical Analysis**

All statistical analyses were performed using ReviewManager version 5.3. We used a random-effects model for meta-analysis and expressed treatment effects as a risk ratio with 95% confidence intervals (CI) for dichotomous outcomes and mean difference with 95% CI for continuous outcomes. An  $l^2 > 50\%$  indicated a large heterogeneity not explained by chance.

### Results

## **Description of Included Studies**

1585 studies were cited as relevant articles after database searching. Repeated, unreported renal function, case reports, reviews, or meta-analysis was excluded after reading the title and abstract. Sixty-one articles were screened for intensive reading. Twelve articles were excluded because of no follow-up rate, no available data, or based on the same study population. Finally, 49 studies were incorporated into the meta-analysis [7–9, 16–61]. A flow diagram displaying the process of selecting the included studies is illustrated in Fig. 1. And the baseline study and patients' characteristics are outlined in Table 1.

## **Quality Assessment of Included Studies**

Newcastle–Ottawa scale was used to evaluate the quality of the included studies. Total score of each document ranges from 4 to 9. And the total score of all studies was not less than 3 (3 represents low quality). Totally 49 studies were all incorporated into the meta-analysis.

## **Meta-analysis Results**

#### GFR

GFR was assessed in 33 out of 49 studies pre- and postoperative; 6 articles were excluded because their results were inconsistent with other studies. GFR increased after BS in 22 out of 27 studies, while decreased in the remaining 5 studies. Twenty-seven studies involving 3157 patients were integrated into meta-analysis of GFR. There was no significant





by 13.81 ml/min/1.73 m<sup>2</sup> (95% CI, 10.31 to 17.32 ml/ min/1.73 m<sup>2</sup>). For the GFR > 120 subgroup (hyperfiltration subgroup), the post-operative GFR decreased by 9.61 (95% CI, – 16.31 to – 2.91 ml/min/1.73 m<sup>2</sup>) (Fig. 2). Also, there was no statistically significant of the pre- and post-operative changes in GFR, with or without diabetes, no matter how the surgical technique (RYGB, SG, or LAGB) had been taken (Supplemental Fig. 1). There was a biggest increase of GFR (MD 14.27 ml/min/1.73 m<sup>2</sup>) in 6–12 months after BS. Postoperative GFR of 6 months, 2 years, and 5–10 years increased 9.53, 7.37, and 6.02 ml/min/1.73 m<sup>2</sup>, respectively (Fig. 7A and Supplemental Fig. 2).

difference in GFR changes after BS in the analysis between the overall group (MD,  $3.08 \text{ ml/min}/1.73 \text{ m}^2$ ; 95% CI, -1.35



Table 1 General c	haracteristics of in	cluded studies								
Study	Country	Design	Surgical tech- nique	No. of patients	Female	Age	Baseline BMI	Follow-up	Renal param- eters assessed	GFR method
Khalil et al. [19]	Mansoura, Egypt	Prospective observational	LSG	4	29	32.5±8.9	50.6±6.7	6 m	Microalbumi- nuria, eGFR, serum creati- nine	CKD-EPI
Kim and Kim [8]	Seoul, Korea	Retrospective observational	RYGB, SG	136	101	35.9±11.2	39.9±6.3	1 y	eGFR, UACR, UPCR, micro- albuminuria, creatinine	MDRD: the Modi- fication of Diet in Renal Disease formula
McIsaac et al. [17]	Saskatoon, Canada	Observational retrospective cohort	RYGB, LSG	471	380	46±10	47.7±7.8	1–2 y	uACR, eGFR, albuminuria	CKD-EPI
Friedman et al. [18]	USA	Prospective observational	RYGB, LAGB, others	737	520	52 (44, 58)	46 (42, 52)	5 y	eGFR, UACR, albuminuria	CKD-EPI equa- tion
Bjornstad et al. [16]	USA	Prospective observational	RYGB	557	422	1	~	1–5 y	¢GFR, UACR	FAS combined serum creatinine and cystatin C equation
Brix et al. [20]	Vienna, Austria	Cross-sectional/ longitudinal intervention	RYGB, SG, GB	318	245	40±12	45.6±6.6	2 y	Albuminuria, creatinine	
Saeed et al. [9]	New York, USA	Retrospective	RYGB, SG	2247	2000	37 (18–76)	45±7	3 y	eGFR, UACR, albuminuria, creatinine	NA
Young et al. [21]	USA	Retrospective	RYGB, SG	101	56	53 (土11)	33.8 (土 8.3)	61 (±29) m	Albuminuria, uACR, serum creatinine	
Park et al. [22]	Seoul, South Korea	Prospective cohort study	RYGB, SG	43	40	32 (26-45)	36.9 (34.0-42.8)	6 m	eGFR, uACR, serum creati- nine	CKD-EPI
Billeter et al. [23]	German	Prospective	RYGB	20	10	58.6±6.1	32.8±2.1	1–2 y	eGFR, UACR, serum creati- nine, cystatin C, CKD-EPI creatinine- cystatin C clearance	MDRD
Nehus et al. [24]	NSA	Prospective multicenter	RYGB, SG, LAGB	242	183	17.1	50.5 (45.2, 58.3)	6 m–3 y	eGFR, albumi- nuria, ACR	Cystatin C-based Larsson formula
Neff et al. [25]	Lille, France	Prospective cohort study	RYGB, LAGB	461	364	43±1 (RYGB)/41±1 (LAGB)	50±1 (RYGB)/47±1 (LAGB)	1–5 y	eGFR	MDRD, CKD- EPI, Cockcroft- Gault formulae

Table 1 (continue	(p									
Study	Country	Design	Surgical tech- nique	No. of patients	Female	Age	Baseline BMI	Follow-up	Renal param- eters assessed	GFR method
Holcomb et al. [7]	USA	Retrospective	RYGB, SG	149	126	$44.3 \pm 10.9$	$48.7 \pm 9.1$	2 y	eGFR, serum creatinine	CKD-EPI
Garcia et al. [26]	Brazil	Prospective cohort study	RYGB	109	84	$38.3 \pm 10.3$	$36.7 \pm 3.6$	1 y	eGFR, serum creatinine	CKD-EPI
Solini et al. [27]	Italy	Prospective	RYGB	25	19	46.7±12.9	<b>44.8±6.0</b>	1 y	Creatinine, eGFR, mGFR	eGFR: CKD-EPI, mGFR: plasma iohexol clear- ance
Hung et al. [28]	Taiwan, China	Retrospective cohort study	RYGB, SG, Others	252	139	$40.5 \pm 11.2$	$39.0 \pm 5.5$	1 y	eGFR, serum creatinine	CKD-EPI
Hou et al. [29]	China	Retrospective	RYGB, SG, LAGB, miniGB	233	184	<b>33.1±9.7</b>	<b>39.5±9.7</b>	1 y	Creatinine, eGFR	MDRD 4-variable formula
Mirajkar et al. [30]	UK	Retrospective cohort	RYGB, SG, LAGB	163	109	$48.5 \pm 8.8$	$50.8 \pm 9.1$	1.3 9.9 y	eGFR	MDRD
Reid et al. [31]	USA	Retrospective	RYGB, SG	158	145	$40.8 \pm 0.9$	47.0±0.6	1 y	Creatinine, eGFR, UACR	CG formula modified for obese subjects using lean body weight
Fenske et al. [32]	UK	Prospective	RYGB, SG, LAGB	34	29	35–54 y	44.6±0.9	1 y	Creatinine, cys- tatin C, eGFR, UACR	MDRD
Navaneethan and Yehnert [33]	USA	Retrospective	Any form	25	18	51.5±7.4	49.8±7.5	6–12 m	Creatinine, eGFR	MDRD 4-variable formula
De Paula et al. [34]	Brazil	Prospective RCT	SG	38	11	53.3±7.7	$28.9 \pm 3.2$	>2 y	Albuminuria	1
Zakaria et al. [ <b>35</b> ]	Milano, Italy	Retrospective	AGB	20	17	44.7±9.5	42.8±4.9	13.8±2.04 y	eGFR, creatinine	NA
Ngoh et al. [36]	Singapore	Retrospective	GB, SG	68	44	40.7±10.8	41.9±5.7	1 y	Creatinine, eGFR	CKD-EPI, CG- LBW, aGFR (absolute GFR) = eGFR by CKD-EPIxBSA
Miras et al. [37]	London, UK	Prospective case-control	RYGB	70	17	$50.7 \pm 1.0$	43.6 (40.6–49.7)	12–18 m	uACR	1
Chagnac et al. [38]	Israel	Prospective cohort	Gastroplasty	8	4	36±2	48.0±2.4	12–17 m	mGFR	Inulin clearance

Table 1 (continue	(p:									
Study	Country	Design	Surgical tech- nique	No. of patients	Female	Age	Baseline BMI	Follow-up	Renal param- eters assessed	GFR method
Zhang et al. [39]	China	Retrospective	RYGB	101	45	<i>47.</i> 6±11.9	30.5 ±3.05 (DN1); (DN1); 30.1 ± 2.89 (DN2); 31.7 ± 3.86 (DN3); 31.72 ± 3.20 (DN4)	1 y	mGFR, ACR, 24-h alblumi- nuria, serum creatinine	99mTc-DTPA
Stephenson et al. [40]	Australia	Retrospective	LAGB	23	11	58±9	$40.1 \pm 5.4$	3 y	uACR	1
Abouchacra et al. [41]	United Arab Emirates	Retrospective cohort	Bariatric surgery	220	145	34.7±10	47±9	6 m	eGFR, creatinine	MDRD, CKD-EPI
Amor et al. [42]	Spain	Prospective	RYGB, SG	255	0.71	$45.6 \pm 10.6$	47.7±6	2 y	UACR, creati- nine	1
DePaula et al. [43]	Brazil	NA	II-DSG	69	22	51.4±5.6	$25.7 \pm 1.9$	>1 y	Microalbumi- nuria	1
Getty et al. [44]	USA	Prospective	RYGB	37	30	47 ± 11	47.6±6.3	6 m	Creatinine, eGFR	MDRD, creati- nine clearance, Cockcroft-Gault equation
Saliba et al. [45]	USA	Prospective	RYGB	35	31	T2DM, 45±9; non-T2DM, 42±10	T2DM, 47±8; non-T2DM, 48±8	12 m	Creatinine, eGFR, proteinuria, albuminuria	Creatinine clear- ance (24-h urine creatinine, plasma creati- nine)
Zeve et al. [46]	Brazil	Prospective cohort	RYGB	17	10	Mean 44.9	44.3±1.3	12 m	Crcl, proteinuria, microalbumi- nuria	Creatinine clear- ance
Luaces et al. [47]	Spain	Prospective	RYGB, tubular gastrectomy	61	50	41.1±9.8	47.4±5	12 m	Creatinine, eGFR	CG-LBW equa- tion
Jose et al. [48]	UK	Retrospective	BPD	25	17	$42.8 \pm 11.3$	57.3±12.6	3.9 years (2–6)	Creatinine, eGFR	MDRD
Mohan et al. [49]	USA	Retrospective	RYGB	38	34	$41 \pm 10.3$	46±8	1 m	uACR	/
Navaneethan et al. [50]	USA	Prospective	RYGB, SG, LAGB	15	9	51.2±14.3	48.8±9.4	6 m	Creatinine, cys- tatin C, UACR	/

Table 1 (continue	ed)									
Study	Country	Design	Surgical tech- nique	No. of patients	Female	Age	Baseline BMI	Follow-up	Renal param- eters assessed	GFR method
Friedman et al. [51]	USA	Prospective	Not mentioned	36	28	50±11	46 ± 9	Mean 10 m	Creatinine, cys- tatin C, mGFR, eGFR	mGFR: plasma iohexol clear- ance; eGFR: MDRD, CKD-EPlcreat, CKD-EPlcreat- cystC, cystC
Lieske et al. [52]	USA	Prospective cohort study	RYGB, BPD	Ξ	11	49.5±11.5	45.7±5.0	12 m	mGFR (iothala- mate clear- ance), eGFR (CKD-EPI), Crcl	mGFR: iothala- mate clearance, eGFR: CKD- EPI
Ruiz-Tovar et al. [53]	Spain	Prospective	DSJ	50	4	$49.2 \pm 6.4$	48.4±7.7	12 m	Creatinine, eGFR	MDRD
Navarro-Diaz et al. [54]	Spain	Prospective con- trolled study	Fobi pouch GB, vertical- banded gastro- plasty	61	37	41.10±9.07	53.62±9.65	2 y	Creatinine, eGFR, proteinuria, albuminuria	Creatinine clear- ance
Palomar et al. [55]	Spain	Prospective	BPD	35	9	$40.1 \pm 11.6$	$46.9 \pm 6.3$	12 m	Proteinuria, albuminuria	1
Iaconelli et al. [56]	Italy	Case-control	BPD	22	12	43.8±8.3	$50.47 \pm 8.46$	10 y	24-h albuminu- ria, creatinine	1
Heneghan et al. [57]	USA	Retrospective cohort	RYGB, SG, AGB	52	39	$51.2 \pm 10.1$	49±8.7	5 y	24-h alblumi- nuria, uACR, creatinine	1
Celik et al. [58]	Netherlands	Retrospective	RYGB	33	31	45.2±8.5	44.6±5.4	21 m	ACR, 24-h albluminuria	/
Schuster et al. [59]	NSA	Retrospective	RYGB	813	626	$45 \pm 10$	NA	≥2 y	Creatinine	1
Agrawal et al. [60]	USA	Retrospective	RYGB	94	72	$45.6 \pm 10.5$	$49.1 \pm 8.0$	12 m	Creatinine, UACR	1
Serpa Neto et al. [61]	Brazil	Retrospective	RYGB	140	96	18-60	$46.17 \pm 5.44$	8 B	Creatinine, eGFR, proteinuria, albuminuria	Creatinine clear- ance (24-h urine creatinine, plasma creati- nine)

	pos	t-surge	ry	pre	surgery	/		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
7.1.1 All study	04.2	25.4	20	96.0	01 E	20	2 50/	9 10 [ 10 05 06 05]	
Zakariaz016	94.3	35.4	20	86.Z	21.5	20	2.5%	8.10 [-10.05, 26.25]	
Sorna Noto2000	112.9	10.Z	25	00.9	10.2	140	3.5%	22.10 [12.00, 31.40]	
Serpa Nelozoog	77.6	31.7	140 50	140.75	33.27	140	3.1%	-54.95 [-42.81, -27.09]	
Ruiz-Tovarzo15	07.1	15.2	150	02.5	14.0	150	3.9%	10.10 [9.20, 20.94]	
Reluzu 14 Park 2018	120.2	126	130	97.0	2.Z	100	4.2%	-10.40 [-10.66, -9.94] 4 50 [ 1 71 10 71]	
Nikhil Miraikar2016	120.2 88.8	12.0	163	86.5	20.8	163	J.9%	2 30 [ 2 01 6 61]	÷-
Nikilii Wilajkai 2010	102	10.9	68	108	20.0	69	3 8%	6 00 [ 12 30 0 30]	
Nobus2017	115	20	197	100	27	238	3.0%	7 00 [1 61 12 30]	
Noff2017	03	23	271	88	27 1	200	4.2%	5 00 [4 73 5 27]	
Navaneethan2009	61.6	16 7	25	47 9	10.2	25	3.7%		
McIsaac2019	106.2	27	182	107.5	10.2	471	4.0%	-1 30 [-5 34 2 74]	+
uaces2012	95.7	23.4	61	92.7	25.1	61	3.6%	3 00 [-5 61, 11 61]	
ieske2014	90	16	11	84	20	11	2.8%	6.00 [-9.14, 21.14]	
Kim2016	119.6	15.3	136	117.8	14.9	136	4 1%	1 80 [-1 79 5 39]	+
Khalil2020	108.4	14.4	44	103	14.8	44	3.9%	5 40 [-0 70 11 50]	
Hung2020	101.3	19.2	252	106.2	10.2	252	4 1%	-4 90 [-7 58 -2 22]	+
Hou2013	114.2	22.2	127	105.2	9.6	127	4.1%	8 50 [4 29 12 71]	-
Holcomb2018	00.5	24.0	1/10	03.0	25.4	149	3.0%	5 60 [-0 11 11 31]	
Setty2012	104.9	23.5	37	91.6	20.4	37	3.2%	13 30 [1 10 25 50]	
Sarcia2020	104.9	16.4	100	91.0	10	100	0.2 /0 4 ∩%	8 50 [3 70 13 21]	
Friedman2014	904	21	36	33.3 87	20	36	3.5%		
Fenske2013	90 85	21	3/	67 /	20	34	4 2%	17 60 [16 85 18 35]	· · ·
Chagnac2003	110	2 7	Э4	1/5	1/	54 Q	- <b>⊤.∠</b> /0 3,30/	-35 00 [-45 85 -24 15]	
Biorpstad2020	110	21 59	129	108.8	28 51	2/1	3.0%	-320 [ 1 80 8 20]	
Bjumstauzuzu Billotor2016	111 7	21.00	20	06.4	20.01	241	2.5%	15 30 [-0.00, 31 50]	
Abouchacra2013	110.7	23.3	20	107.8	20.7	20	2.7 /0	2 90 [-4 92 10 72]	
Subtotal (95% CI)	110.7	47	2714	107.0	50	3157	100 0%	3 08 [-1 35 7 52]	•
Hotorogonoity: Tau <sup>2</sup> -	122 02. (	2hi2 - 54	107.20	df - 26	(D < 0 0	0001)	12 - 0.00/	0.00 [1.00, 1.02]	ť
Test for overall effect:	Z = 1.36	(P = 0.1	7)						
1.1.2 GFR<90 group									
Nikhil Mirajkar2016-4	85.4	4.5	25	78	6.9	25	12.0%	7.40 [4.17, 10.63]	
Nikhil Mirajkar2016-3	72.5	18.7	4	46.5	9.5	4	2.4%	26.00 [5.45, 46.55]	
Nikhil Mirajkar2016-2	56.4	9.7	11	48.4	9.4	11	7.9%	8.00 [0.02, 15.98]	
Nikhil Mirajkar2016-1	84.1	13.7	44	76.7	8.1	44	10.7%	7.40 [2.70, 12.10]	-
Nikhil Mirajkar2016	79.6	19.7	5	75.2	8.8	5	2.7%	4.40 [-14.51, 23.31]	·
Nehus2017	102	28	48	76	12	59	7.5%	26.00 [17.51, 34.49]	_
Neff2017	68	/	19	52	2	19	11.9%	16.00 [12.73, 19.27]	
Hung2020	82.4	24.7	44	72.6	16.3	76	7.7%	9.80 [1.63, 17.97]	
Hou2013 (<60)	66.8	19.3	6	49.5	6.6	6	3.4%	17.30 [0.98, 33.62]	
Hou2013	93.3	20.4	39	76.8	16.7	39	7.6%	16.50 [8.23, 24.77]	
Holcomb2018	81.6	24.5	62	68.9	15.6	62	8.5%	12.70 [5.47, 19.93]	
Garcia2020	90.6	15.3	41	75.8	11.6	41	9.7%	14.80 [8.92, 20.68]	
Abouchacra2013	103.6	19	41	80.99	18	41	7.9%	22.61 [14.60, 30.62]	
Heterogeneity: Tau <sup>2</sup> =	24.00; CI	hi² = 40.	389 .14, df =	= 12 (P <	0.0001	432 ); l <sup>2</sup> = 7	100.0% 70%	13.81 [10.31, 17.32]	•
Test for overall effect:	Z = 7.72	(P < 0.0	0001)						
likhil Miraikar2016 2	group 05 0	10 0	26	102 7	70	26	11 00/	6 00 [ 12 00 1 00]	<b>_</b>
Niki III IVIIrajkar2016-3	95.8	13.8	30	102.7	1.3	30	11.9%	-0.90 [-12.00, -1.80]	
NIKTIII IVIITAJKAT2016-2	100.3	15	4	103.8	9.1	4	3.8%	-3.50 [-20.69, 13.69]	
NIKAII IVIIrajkar2016-1	100.8	14.1	17	99.5	9.7	1/	9.0%	1.30 [-6.84, 9.44]	1
Ngon2016	113	13	58	115	12	58	12.4%	-2.00 [-6.55, 2.55]	1
venuszu1/	119	28	136	118	21	179	11.4%	1.00 [-4.62, 6.62]	_
1ung2020	101.3	19.2	107	106.2	10.2	1/6	12.9%	-4.90 [-8.84, -0.96]	-  _
1002013	114.2	22.2	127	105.7	9.6	127	12.7%	8.50 [4.29, 12.71]	<u>↓</u> -
	112.6	16.9	87	111.9	13.3	87	12.4%	0.70 [-3.82, 5.22]	Ι_
Sarcia2020	108.9	8.3	52	102.4	8	52	13.6%	6.50 [3.37, 9.63]	
Heterogeneity: Tau <sup>2</sup> =	26.77; Cl	$hi^2 = 43.$	624 .69, df =	= 8 (P <	0.00001	736 );  ² = 8	100.0% 32%	0.44 [-3.46, 4.35]	Ţ
est for overall effect:	∠ = 0.22	(۳ = 0.8	)						
1.1.4 GFR>120		10.0	-	100.0			10 00:		
NIKHII Mirajkar2016	111.4	19.3	8	128.3	7.8	8	16.3%	-16.90 [-31.32, -2.48]	
Hou2013	133.9	25.7	61	146.4	17.1	61	35.0%	-12.50 [-20.25, -4.75]	
Garcia2020	118.2	9.8	16	123.3	2	16	48.7%	-5.10 [-10.00, -0.20]	
Subtotal (95% CI)			85	a (B -		85	100.0%	-9.01 [-10.31, -2.91]	▼
Heterogeneity: Tau <sup>2</sup> = Fest for overall effect: 2	17.74; Cl Z = 2.81	hi² = 4.1 (P = 0.0	0, df = 05)	2 (P = 0	.13); l² =	51%			

◄Fig. 2 Forest plot comparing GFR between presurgery and postsurgery

#### Serum Creatinine

A total of 33 studies reported before-and-after changes on serum creatinine; 5 articles were excluded due to their data

were not compatible with other studies. The concentration of serum creatinine decreased in the overall group after BS (MD, -0.07 mg/dl; 95% CI, -0.09 to -0.05 mg/dl). Only GFR > 90 subgroup (no CKD subgroup), serum creatinine increased by 0.02 mg/dl (95% CI, 0.00 to +0.04 mg/dl) (Fig. 3). Compared with RYGB (MD, -0.08 mg/dl; 95% CI, -0.15 to 0.00 mg/dl), SG (MD, -0.13 mg/

	post	t-surge	ry	pre-	surge	ry		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.1.1 All study									
Abouchacra2013	0.58	0.13	220	0.63	0.14	220	5.7%	-0.05 [-0.08, -0.02]	-
Agrawal2008	0.8	0.2	25	0.9	0.2	25	2.5%	-0.10 [-0.21, 0.01]	——————————————————————————————————————
Billeter2016	0.69	0.13	20	0.82	0.23	20	2.4%	-0.13 [-0.25, -0.01]	
Fenske2013	0.77	0.02	34	0.84	0.02	34	6.1%	-0.07 [-0.08, -0.06]	•
Friedman2014	0.72	0.17	36	0.81	0.24	36	3.0%	-0.09 [-0.19, 0.01]	
Garcia2020	0.75	0.2	109	0.84	0.2	109	4.6%	-0.09 [-0.14, -0.04]	
Getty2012	0.72	0.16	37	0.83	0.21	37	3.3%	-0.11 [-0.20, -0.02]	
Holcomb2018	0.853	0.43	149	0.895	0.31	149	3.3%	-0.04 [-0.13, 0.04]	
Hou2013	0.78	0.7	127	0.75	0.1	127	2.2%	0.03 [-0.09, 0.15]	
Hung2020	0.75	0.16	107	0.71	0.12	176	5.4%	0.04 [0.00, 0.08]	-
Jose2013	0.8	0.16	25	0.98	0.17	25	3.1%	-0.18 [-0.27, -0.09]	
Khalil2020	0.87	0.1	44	0.97	0.16	44	4.5%	-0.10 [-0.16, -0.04]	
Lieske2014	0.7	0.1	11	0.8	0.2	11	2.0%	-0.10 [-0.23, 0.03]	
Luaces2012	0.69	0.11	61	0.71	0.15	61	4.9%	-0.02 [-0.07, 0.03]	
McIsaac2019	0.67	0.18	182	0.62	0.16	471	5.6%	0.05 [0.02, 0.08]	
Navaneethan2009	1.1	0.3	25	1.4	0.4	25	1.1%	-0.30 [-0.50, -0.10]	
Navaneethan2010	0.64	0.1	15	0.78	0.21	15	2.3%	-0.14 [-0.26, -0.02]	
Navarro-Dı'az2006	0.83	0.13	61	0.91	0.13	61	4.9%	-0.08 [-0.13, -0.03]	
Ngoh2016	0.72	0.28	68	0.73	0.3	68	2.9%	-0.01 [-0.11, 0.09]	
Reid2014	0.67	0.1	158	0.72	0.1	158	5.8%	-0.05 [-0.07, -0.03]	+
Ruiz-Tovar2015	0.71	0.14	50	0.89	0.17	50	4.3%	-0.18 [-0.24, -0.12]	
Saeed 2020	0.7	0.2	191	0.8	0.2	2247	5.6%	-0.10 [-0.13, -0.07]	-
Saliba2010	0.63	0.09	19	0.64	0.11	19	4.2%	-0.01 [-0.07, 0.05]	
Schuster2011	1.2	0.6	21	1.42	0.14	40	0.7%	-0.22 [-0.48, 0.04]	
Serpa Neto2009	0.69	0.13	140	0.83	0.2	140	5.2%	-0.14 [-0.18, -0.10]	
Solini2019	0.76	0.22	25	0.76	0.19	25	2.4%	0.00 [-0.11, 0.11]	<del></del>
Zakaria2016	0.699	0.265	20	0.767	0.26	20	1.5%	-0.07 [-0.23, 0.09]	
ZEVE2013	0.9	0.1	17	0.9	0	17		Not estimable	
Zhang2015	0.56	0.9	34	0.62	0.16	34	0.5%	-0.06 [-0.37, 0.25]	
Subtotal (95% CI)			2031			4464	100.0%	-0.07 [-0.09, -0.05]	$\bullet$
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <sup>2</sup> = 159	.26, df	= 27 (F	< 0.00	0001); I	² = 83%		
Test for overall effect:	Z = 5.96	(P < 0.0	00001)	``		,,			
			,						
2.1.2 GFR<90 group	)								
Abouchacra2013	0.76	0.13	41	0.8	0.14	41	29.6%	-0.04 [-0.10, 0.02]	
Holcomb2018	1.03	0.62	62	1.11	0.36	62	7.7%	-0.08 [-0.26, 0.10]	
Hou2013	0.8	0.1	39	0.9	0.1	39	34.6%	-0.10 [-0.14, -0.06]	-
Hou2013 (<60)	1.2	0.3	6	1.4	0.2	6	3.3%	-0.20 [-0.49, 0.09]	
Hung2020	1	0.3	44	1	0.4	76	13.2%	0.00 [-0.13, 0.13]	
Navaneethan2009	1.1	0.3	25	1.4	0.4	25	6.6%	-0.30 [-0.50, -0.10]	
Ngoh2016	0.96	0.25	10	1.1	0.27	10	5.1%	-0.14 [-0.37, 0.09]	
Subtotal (95% CI)			227			259	100.0%	-0.09 [-0.14, -0.03]	$\bullet$
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <sup>2</sup> = 9.88	8, df =	6 (P = 0	).13); l <sup>a</sup>	² = 39%			
Test for overall effect:	Z = 3.09	(P = 0.0	002)		,				
2.1.3 GFR>90									
Holcomb2018	0.728	0.12	87	0.737	0.12	87	28.0%	-0.01 [-0.04, 0.03]	*
Hou2013	0.61	0.13	61	0.58	0.1	61	21.4%	0.03 [-0.01, 0.07]	<b>†</b> ■-
Hou2013 (<60)	0.78	0.7	127	0.75	0.1	127	2.5%	0.03 [-0.09, 0.15]	<del></del>
Hung2020	0.75	0.16	107	0.71	0.12	176	28.9%	0.04 [0.00, 0.08]	
Ngoh2016	0.59	0.12	58	0.58	0.12	58	19.1%	0.01 [-0.03, 0.05]	+
Subtotal (95% CI)			440			509	100.0%	0.02 [-0.00, 0.04]	•
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <sup>2</sup> = 4.20	0, df = -	4 (P = 0	).38); l <sup>a</sup>	² = 5%			
Test for overall effect:	Z = 1.81	(P = 0.0	07)						

Fig. 3 Forest plot comparing creatinine between presurgery and postsurgery



Fig. 4 Forest plot comparing ACR between presurgery and postsurgery

dl; 95% CI, -0.18 to -0.08 mg/dl) has better effect in reducing serum creatinine (Supplemental Fig. 3). There was no significant difference in pre- and post-operative changes of serum creatinine between the two groups of patients with and without diabetes (Supplemental Fig. 3). Although creatinine dropped the most in 3–5 years after BS (MD, -0.11 mg/dl; 95% CI, -0.16 to -0.07 mg/dl), it was no significantly decrease (p=0.27) in the following period: 6 months (MD, -0.08 mg/dl; 95% CI, -0.12 to -0.04 mg/dl), 1 year (MD, -0.06 mg/dl; 95% CI, -0.09 to -0.03 mg/dl), or 2 years follow-up (MD, -0.06 mg/dl; 95% CI, -0.14 to -0.03 mg/dl) (Fig. 7B and Supplemental Fig. 4).

#### ACR

Only 8 studies with available data were for ACR out of 49 included studies. ACR be slightly increased in 2 out of 8 studies, while reduced in the remaining 6 studies. It had been decreased in the overall group (MD, -12.46 mg/g; 95% CI, -20.11 to -4.82 mg/g) (Fig. 4) and all subgroups after BS. Reductions in ACR were seen after RYGB or SG and in patients with or without diabetes (Supplemental Fig. 5). There was no significant difference in pre- and post-operative changes

of ACR for all subgroups. It also declined most significantly at 1 year (MD, -18.03 mg/g; 95% CI, -27.35 to -8.71 mg/g) and 2 years (MD, -18.20 mg/g; 95% CI, -29.20 to -7.19 mg/g) after BS (Fig. 7C and Supplemental Fig. 6).

#### Albuminuria

Twenty-three out of 49 studies had albuminuria inspection pre- and post-operative. It had significantly improved in all other studies except for one that did not change. There was a statistically significant reduction in the incidence of albuminuria after bariatric surgery (RR: 0.40, 95% CI: 0.31–0.51, p < 0.0001;  $I^2 = 71\%$ ) (Fig. 5). A decrease in albuminuria was noted after BS (MD, – 14.17 mg/day; 95% CI, – 22.59 to – 5.76 mg/day) (Fig. 6).

## Discussion

Evidence from this meta-analysis shows an improvement in renal function after bariatric surgery. First, although the change of GFR was inconsistent in all included studies, it decreased in patients with hyperfiltration while increased

	pos	stsurgery	/	pres	surgery			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Khalil2020	14	10	44	23	19	44	16.2%	-9.00 [-15.34, -2.66]	+
Lieske2014	17.1	10.8	11	20.5	10.4	11	14.9%	-3.40 [-12.26, 5.46]	
Saliba2010	15	29	19	26	50	19	6.6%	-11.00 [-36.99, 14.99]	
Saliba2010-1	14	20	16	10	6	16	14.1%	4.00 [-6.23, 14.23]	
ZEVE2013	39.7	21.4	17	120.8	46.9	17	7.1%	-81.10 [-105.61, -56.59]	
Zhang2015	9.97	4.48	31	15.95	11.37	31	17.0%	-5.98 [-10.28, -1.68]	•
Zhang2015-1	8.46	4	34	13.26	7.89	34	17.4%	-4.80 [-7.77, -1.83]	-
Zhang2015-2	17.94	14.73	21	83.73	59.13	21	6.6%	-65.79 [-91.85, -39.73]	
Zhang2015-3	513.46	730.36	15	1,052.32	954.77	15	0.0%	-538.86 [-1147.19, 69.47]	· · · · · · · · · · · · · · · · · · ·
Total (95% CI)			208			208	100.0%	-14.17 [-22.59, -5.76]	◆
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:	103.42; 0 Z = 3.30	Chi² = 64. (P = 0.00	.85, df = 10)	= 8 (P < 0.0	00001); F	² = 88%	)		-100 -50 0 50 100



in patients with reduced eGFR (CKD). Second, serum creatinine level decreased significantly after BS in the overall group, while it increased slightly in the subgroup with GFR > 90. But it still keeps in the normal range. Third, data on changes pre- and post-operative indicated that ACR and albuminuria decreased significantly after bariatric surgery. Fourth, renal function improved the most in 1–2 years after bariatric surgery (Fig. 7).

GFR is the product of functional nephrons' quantity which remains constant after birth and the filtration rate of single nephron [62]. Healthy kidney has functional renal reserve, i.e., not all nephrons are activated in normal physiological states. And some nephrons are in idle state [63]. Early obesity leads to the decrease of functional renal reserve which activated the motionless nephrons. It makes the body show hyperfiltration [64]. Nevertheless, long-term hyperfiltration will reduce the filtration of single nephron declining the total GFR, and eventually leads to kidney damage [65]. Therefore, hyperfiltration may be reversible because of the renal functional reserve. Whether the decrease or increase in post-operative GFR results from an improvement in hyperfiltration or a real renal function is uncertain. It is illogical to judge the effect of bariatric surgery on renal function only based on the rising and falling of GFR. For obese patients with normal renal reserve function, bariatric surgery was initially to redress the hyperfiltration caused by obesity and maintain the normal number of activated nephrons. So, GFR showed a downward tendency. For patients who activated all nephrons with renal insufficiency and reserve function dysfunction, in this condition, the effect of bariatric surgery on renal function can be truly reflected from the change of total GFR. And the increase in total GFR is necessarily the result of the growing of filtration rate of single nephron. Our meta-analysis demonstrates that bariatric surgery can reduce the GFR of patients with hyperfiltration and increase the GFR of patients with renal insufficiency, which is the favorable evidence for bariatric surgery to enhance renal function.

Serum creatinine levels are usually relatively normal due to renal reserve function until about 50% of nephrons be invalidated or GFR drops to nearly 60 ml/min/1.73 m<sup>2</sup> [66]. Therefore, when GFR > 60 ml/min/1.73 m<sup>2</sup>, serum creatinine is not an accurate indicator of renal function. But the level of serum creatinine to some extent reflects the capability of the kidney to clean up metabolic waste. Serum creatinine is maintained at a normal level, indicating that the renal clearance function can meet the metabolic needs. Moreover,

	post-sur	gery	pre-sur	gery		<b>Risk Ratio</b>		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Ranc	lom, 95% Cl	
Agrawal2008	6	94	21	94	3.9%	0.29 [0.12, 0.68]				
Amor2013	11	96	44	96	5.3%	0.25 [0.14, 0.45]				
Billeter2016	1	19	4	20	1.1%	0.26 [0.03, 2.15]		· · · ·	<u> </u>	
Brix2019	27	318	56	318	6.3%	0.48 [0.31, 0.74]		-		
Celik2013	3	31	3	32	1.9%	1.03 [0.23, 4.73]				
DePaula2009	7	69	69	69	4.8%	0.11 [0.05, 0.21]				
Friedman2014	81	468	141	650	7.3%	0.80 [0.62, 1.02]		-	1	
Heneghan2013	8	19	19	19	5.8%	0.44 [0.26, 0.73]				
Hou2013	34	84	55	84	7.1%	0.62 [0.46, 0.84]		-		
laconelli2011	2	22	7	22	2.0%	0.29 [0.07, 1.23]			t	
Khalil2020	2	44	17	44	2.1%	0.12 [0.03, 0.48]				
Kim2016	6	136	30	136	4.0%	0.20 [0.09, 0.46]				
Miras2015	15	70	30	70	5.8%	0.50 [0.30, 0.84]		_		
Navarro-Dı´az2006	3	15	7	15	2.8%	0.43 [0.14, 1.35]			+	
Nehus2017	10	61	16	61	4.7%	0.63 [0.31, 1.27]			+	
Palomar2005	19	173	39	230	5.8%	0.65 [0.39, 1.08]		-	t	
Park2018	1	35	15	35	1.2%	0.07 [0.01, 0.48]				
Paula2010	4	43	16	43	3.3%	0.25 [0.09, 0.69]				
Reid2014	4	38	18	38	3.4%	0.22 [0.08, 0.60]				
Saeed 2020	4	158	22	158	3.1%	0.18 [0.06, 0.52]				
Serpa Neto2009	12	191	35	224	5.1%	0.40 [0.21, 0.75]				
Stephenson2013	31	140	61	140	6.7%	0.51 [0.35, 0.73]		-		
Young2019	11	22	23	23	6.4%	0.51 [0.34, 0.77]		-		
Total (95% CI)		2346		2621	100.0%	0.39 [0.30, 0.49]		•		
Total events	302		748							
Heterogeneity: Tau <sup>2</sup> =	0.18; Chi²	= 69.93,	df = 22 (F	<b>&gt;</b> < 0.00	0001); l² = (	69%				100
Test for overall effect:	Z = 7.85 (F	o < 0.000	001)				0.01	U.I		100
			,					post-surgery	pre-surgery	

Fig. 6 Forest plot comparing the incidence of albuminuria between presurgery and postsurgery

Fig. 7 The changes of renal function after bariatric surgery in different postoperative periods. A The GFR difference of preoperative and postoperative in different periods. B The creatinine difference of preoperative and postoperative in different periods. C The ACR difference of preoperative and postoperative in different periods



# A The GFR difference of preoperative and postoperative in different period



B The creatinine difference of preoperative and postoperative in different period





creatinine-based eGFR is not validated in obese individuals because of high muscle quality, which may underestimate renal function in obese individuals [67]. Hence, it is more convincing that the decrease of creatinine level reflects the improvement in renal clearance after BS.

Albuminuria closely relating to all levels of renal function is an important manifestation of renal function damage. There is no question that microalbuminuria is improved after bariatric surgery, whether post-operative remission of preoperative albuminuria or new onset albuminuria. Compared with non-surgical control group, the post-operative microalbuminuria in the operation group reduced significantly after BS. Our results are consistent with previous studies that the incidence of albuminuria, microalbuminuria level, and uACR decreased after BS.

The weight loss caused by BS is the most significant 1 year after operation. Then, the weight regained in different degrees. The optimal benefit time of bariatric surgery on renal function, however, has not been studied. This study first conducts subgroup analysis based on different follow-up periods after bariatric surgery. Considering the early decline of GFR due to improvement of hyperfiltration in patients with preserved renal reserve function, we only included patients with renal insufficiency (GFR < 90) at baseline in the follow-up subgroup analysis of GFR. The maximum increase of GFR is noted during 6-12 months after BS. And serum creatinine achieved the most noticeable decrease in 3-5 years after BS (although no significant difference). These are inconsistent with the trajectory of weight loss after BS. So, it has yet to be further proved that bariatric surgery can not only benefit from weight loss, but also enhance renal function through other mechanisms.

Our research has some limitations. First, the study is disunity in various literature on the measurement of GFR and whether the GFR is adjusted according to the surface area. Secondly, it is the innovation of this study to explore the optimal benefit time point of renal function after bariatric surgery based on subgroup analysis of follow-up time, but more intuitive research is needed to verify the trajectory of renal function after bariatric surgery. Finally, the conclusion of our article has limited effect, because the included articles are mostly observational single-arm studies and have significant heterogeneity.

## Conclusion

Bariatric surgery can improve renal function in obese patients with kidney dysfunction, it reduces the GFR of patients with hyperfiltration and increase the GFR of patients with renal insufficiency, and the incidence of albuminuria, microalbuminuria level, and uACR decrease after BS. In the future, more intuitive research is needed to investigate the trajectory of renal function after bariatric surgery to verify the optimal postoperative benefit time.

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#### Declarations

Ethics Approval For systematic review and meta-analysis studies, formal consent is not required.

Consent to Participate Does not apply.

Competing Interests The authors declare no competing interests.

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