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Original Article

ORIGINAL ARTICLE

Mid- and long-term renal outcomes after metabolic surgery in a multi-center, multi-ethnic Asian cohort with T2DM

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ABSTRACT

Background. Metabolic surgery is recognized for its effectiveness in weight loss and improving outcomes for individuals with type 2 diabetes mellitus (T2DM). However, its impact on renal function, especially in multi-ethnic Asian populations, remains underexplored. This study investigates mid- and long-term renal outcomes following metabolic surgery in Asian patients with T2DM.
Methods. This retrospective cohort study utilized data from the Asian Diabetes Surgery Study (ADSS), involving T2DM patients aged 20–79 who underwent metabolic surgery from 2008 to 2015. The primary outcome was the change in estimated glomerular filtration rate (eGFR) at 1, 3, and 5 years post-surgery, with adjustments for confounders. Secondary outcomes included changes in chronic kidney disease (CKD) stages and the relationship between weight loss and eGFR changes. Data were analyzed using univariate and multivariable regression analyses, along with the McNemar test.
Results. The study included 1513 patients with a mean age of 42.7 years. The results revealed that a significant improvement in eGFR was observed at 1-year post-surgery (112.4 ± 32.0 ml/min/1.73 m², $P < .001$), with a shift toward less severe CKD stages. However, this improvement was not sustained at 3 and 5 years. No significant correlation was found between weight loss and eGFR changes at 1-year follow-up.
Conclusion. Metabolic surgery significantly improves renal function at 1 year postoperatively in Asian individuals with T2DM, highlighting its potential benefits beyond glycemic control and weight loss. The long-term effects on renal function require further investigation.

Keywords: chronic kidney disease, diabetes, metabolic bariatric surgery, renal outcomes

KEY LEARNING POINTS

What was known:

- T2DM is associated with increased risk of chronic kidney disease (CKD).
- Metabolic surgery has been effective in weight loss and improving T2DM outcomes.
- The impact of metabolic surgery on renal function, particularly in Asian populations with T2DM, is not well-documented.

This study adds:

- Metabolic surgery significantly improves renal function as measured by eGFR at 1 year postoperatively in a multi-ethnic Asian cohort with T2DM.
- An overall shift toward less severe stages of CKD in the cohort at 1 year compared to baseline was observed.

Potential impact:

- Suggests metabolic surgery as a viable treatment option for improving renal outcomes in T2DM patients at 1 year.
- Highlights the need for additional studies focusing on other renal parameters such as albuminuria and proteinuria.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a prevalent metabolic disease worldwide [1]. It is a critical chronic condition that leads to numerous complications [2]. According to the International Diabetes Federation (IDF), across Asia, the prevalence of diabetes is ~10.5% among adults aged 20–79 years. Countries such as China and India have particularly high numbers of people with diabetes, contributing significantly to the global burden of the disease [3]. T2DM has different disease features in Asian patients compared to those in Western patients. Asians with T2DM tend to be younger, with more abdominal obesity and greater insulin resistance [4]. As such, patients may develop diabetes earlier and face longer-term chronic complications [4]. As a significant contributor to the development of T2DM, obesity prevalence is also rising worldwide, with ~50%–80% of the adult population being overweight or obese in many countries [5].

Metabolic surgery, a form of bariatric surgery, is the most effective weight loss treatment for morbidly obese patients [6]. Notably, increasing evidence has demonstrated the benefits of metabolic surgery for the treatment and prevention of T2DM [7]. The Second Diabetes Surgery Summit (DSS-II) has included metabolic surgery as a recommended standard intervention for individuals with both T2DM and obesity [8]. Such surgical procedures are reported to enhance glucose homeostasis through various mechanisms, including alterations in gut hormones, bile acid metabolism, the microbiota, and glucose metabolism within the gut [9]. Moreover, the metabolic surgery has been shown to have a sustained beneficial effect on blood glucose for up to 20 years [9].

On the other hand, ~40% of diabetic patients develop chronic kidney disease (CKD), which leads to proteinuria and a reduction in estimated glomerular filtration rate (eGFR), posing a significant public health problem [10, 11]. Several previous studies have suggested that together with metabolic improvements, obese patients undergoing bariatric surgeries experience renal function improvements, including reducing proteinuria and improving GFR [12, 13]. Another previous study reported that patients with obesity and renal impairment who underwent bariatric surgery experienced a 58% reduction in the risk of proteinuria and albuminuria and a 54% reduction in the risk of ultrafiltration [14]. In addition, bariatric surgery was associated with improvements in diabetes and hypertension, which are also risk factors for developing CKD [15, 16]. Previous studies have also indicated that the prevalence of CKD in non-hospitalized adults with T2DM was 34.5%–42.3%, and that most CKD cases were identified at the early stage [17]. Although clinical studies and reviews have reported positive effects of bariatric surgery on renal function, as mentioned before, these findings primarily pertain to the general population affected by obesity [12–16, 18, 19]. Specific attention to diabetic patients is lacking in these studies. Further, most research in this field has predominantly centered on the Western population. High-quality evidence is still lacking to support improvements in renal function in T2DM patients after metabolic surgery, particularly in the Asian population.

Despite the high prevalence of T2DM in the Asian population and the significant burden of CKD, research on renal outcomes following metabolic surgery in this specific subgroup is limited. Gaining a greater understanding of the potential benefits of metabolic surgery on renal outcomes could be beneficial for individuals with these conditions. Therefore, this study aimed to evaluate whether metabolic surgery improves renal function and slows the progression of CKD in a multi-center, multi-ethnic Asian cohort of diabetic patients. We hypothesized that metabolic surgery would improve key renal functional parameters in Asian populations with T2DM at follow-up.

MATERIALS AND METHODS

Study design and data source

This retrospective cohort study analyzed data from the extension of the Asian Diabetes Surgery Study (ADSS), a study on diabetes surgery in Asian patients that investigated clinical predictors for successful metabolic surgery (NCT01317979) and recruited a cohort of diabetic patients from different Asian institutions. The included patients represented hospital admissions from six Asian countries, including: Taiwan (Taipei Medical University Hospital, National Cheng Kung University Hospital, Chiayi Christian Hospital, Min-Sheng General Hospital, and Changhua Christian Hospital); Japan (Yotsuya Medical Cube); Singapore (National University Hospital, Tan Tock Seng Hospital, and Khoo Teck Puat Hospital); India (Saifee Hospital); Hong Kong (Prince of Wales Hospital); and Korea (Soonchunhyang University Hospital).

Study population

Consecutive patients with T2DM and aged 20–79 years who underwent metabolic surgery in the previously mentioned institutions between January 2008 and December 2015, had completed at least 1 year of postoperative follow-up, and had data on eGFR were included. Patients with missing age, sex, or eGFR results were excluded. Patients undergoing metabolic surgery were evaluated pre- and postoperatively by a multidisciplinary team of surgeons, physicians, psychologists, clinical nurse specialists, dietitians, and anesthetists in each institution.

Surgical techniques

Decisions on the type of surgery were made collaboratively by both patients and surgeons. Each surgeon's preferences for choice of procedure were not standardized and could be changed over time during the study period. Types of metabolic surgeries performed included: laparoscopic vertical banded gastroplasty, laparoscopic sleeve gastrectomy (SG), laparoscopic Roux-en-Y gastric bypass, laparoscopic single-anastomosis gastric bypass (LSAGB), laparoscopic mini-gastric bypass (LMGB), laparoscopic adjustable gastric banding (LAGB); laparoscopic adjustable gastric banded plication, and duodenojejunal bypass with SG (DJBSG).

Ethics statement

The study protocol was reviewed and approved by the Institutional Review Boards of the respective institutions (IRB No MSIRB2015002, CRE 2010.109, YCR18027, and N201810050). Because patient data were deidentified in this retrospective study, the IRB waived signed informed consent of included patients.

Study variables and outcome measures

The primary outcome was the changes in eGFR at 1, 3, and 5 years postoperatively compared to the baseline measure after adjusting for relevant confounders. The secondary outcomes were: (i) change in the proportion of CKD stages within the study cohort at 1 year postoperatively from baseline; and (ii) correlations between weight loss and eGFR change at 1 year postoperatively from baseline.

Individuals' eGFR values were calculated using the simplified modification of diet in renal disease (MDRD) equation:

$$\mathrm{eGFR}(\mathrm{mL/min}/1.73\,\mathrm{m}^2) = 186 \times (\text{serum creatinine})^{-1.154} \times (\mathrm{Age})^{-0.203} \times (0.742\ \text{if female}).$$

Serum creatinine was measured using the enzymatic method. To guarantee consistent results throughout the study, we adhered to regular calibration protocols recommended by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

Individuals' CKD stage was categorized through eGFR values: stage 1, eGFR $\geq$90; stage 2, 60–89; stage 3A, 45–59; stage 3B, 30–44; stage 4, 1–29; and stage 5, $<$15 ml/min/1.73 m^2.

Patients' baseline characteristics included age (categorized into 20–39 years, 40–59 years, and 60–79 years), sex, country of origin, type of metabolic bariatric surgery received, body composition parameters [i.e. weight, height, body mass index (BMI), waist-to-hip ratio], smoking status, systolic blood pressure (SBP), and whether or not data of major morbidities (defined as any severe, life-threatening, or chronic condition that required medical intervention or hospitalization) were extracted from the medical records. Preoperative DM-related measurements included: duration of DM, fasting glucose and insulin levels, glycated hemoglobin (HbA1), number of oral anti-diabetic drugs, insulin therapy, and c-peptide level. Laboratory measures included creatinine, albumin, blood lipid levels [i.e. total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL)], uric acid, alanine aminotransferase (ALT), and aspartate transaminase (AST).

Statistical analysis

Continuous data are presented as the mean $\pm$ standard deviation (SD). Categorical data are presented as number (%). Comparisons of the distribution of study variables were conducted using analysis of variance. Univariate and multivariate linear regression analyses were used to determine associations between eGFR changes and weight loss percentage at 1 year after surgery. Multivariate model was adjusted for patients' age, sex, and preoperative parameters, including DM duration, hypertension,

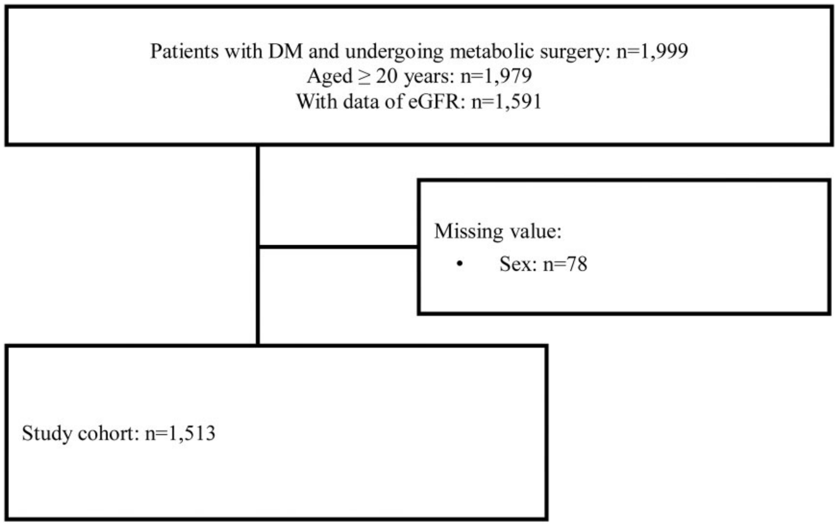

Figure 1: Flow diagram of patient selection.

hyperlipidemia, and glycated hemoglobin (HbA1c). McNemar tests were performed to assess the change in distributions between CKD stage 1–2 and stage 3–5 before and after metabolic surgery. All statistical analyses were performed using the statistical software package SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). A two-sided *P* value of $<.05$ was regarded as statistically significant.

RESULTS

The study cohort selection process is documented in Fig. 1. A total of 1999 patients with DM underwent metabolic surgery. Among them, 1591 patients aged ≥20 years and had data about eGFR. Patients without complete data of age or sex ($n = 78$) were excluded. Finally, 1513 patients were enrolled in the subsequent analyses (Fig. 1).

Characteristics of the study cohort

Table 1 summarizes the preoperative characteristics of the study cohort, including demographic data, patients' body composition parameters, diabetes-related measures, and laboratory parameters. Patients' mean age was 42.7 years. The average mean arterial pressure and HbA1c were 104.9 mmHg and 8.3%, respectively. In total, 857 patients (56.6%) were female, 1249 (82.6%) were recruited in Taiwan, 577 (38.1%) received LSAGB/LMGB, 230 (15.2%) were smokers, and 252 (16.7%) were on insulin (Table 1).

BMI, creatinine, and eGFR of the study cohort over the follow-up period

BMI, creatinine, and eGFR values of the study cohort at baseline and over the follow-up period are shown in Table 2. In brief, 736 patients were followed to 1 year postoperatively, 377 patients to 2 years, 237 patients to 3 years, 129 patients to 4 years, and only 88 patients to 5 years postoperatively. Baseline BMI and eGFR were 38.2 ± 8.0 kg/m^2 and 104.7 ± 31.9 ml/min/1.73 m^2, respectively. At baseline, 5.8% patients had an eGFR < 60. The eGFR was 112.4 ± 32.0, 109.7 ± 28.4, and 108.0 ± 24.2 ml/min/1.73 m^2 at postoperative 1, 3, and 5 years (Table 2).

Distribution of CKD stage of the study cohort at baseline and postoperative 1 year

The data from Table 3 describes the distribution of CKD stages in the study cohort at baseline and one year postoperatively. The proportion of stage 4 CKD dropped from 1.1% to 0.8%, while stage 3B CKD also saw a reduction, dropping from 2.3% to 1.0%. Stage 3A CKD remained relatively stable, with a minor decrease from 2.3% to 2.2%. Stage 2 CKD declined from 20.1% at baseline to 16.4%. Conversely, the proportion of patients with stage 1 CKD increased from 74.2% to 79.5%. Specifically, as shown in green in Table 3, a total of 72 patients moved from stage 2 to stage 1 after surgery, 11 patients from stage 3A shifted to either stage 1 or 2, and 12 patients from stage 3B improved to stages ranging from stage 1 to 3A 1 year postoperatively. The McNemar test indicated that the proportion of patients in stage 1–2 CKD increased from 94.3% to 95.9%, while the proportion of patients in Stages 3–5 dropped from 5.7% to 4.1%, with a statistical significance detected ($P = .011$) (Supplementary Table S1).

Change of eGFR at baseline and at follow-up

The changes in eGFR of the total study cohort and by different subgroups (i.e. age, sex, DM duration, baseline eGFR, baseline hypertension, baseline hyperlipidemia, baseline HbA1c, DM improved, and percentage weight loss) between baseline and 1, 3, and 5 years postoperatively are summarized in Tables 4–6. At 1 year follow-up, after adjusting for confounders, the multivariable analysis showed patients' eGFR was significantly improved compared to the baseline value (112.4 ± 32.0 vs. 106.4 ± 31.7, $P < .001$). In addition, the 1-year eGFR was also significantly improved in most subgroups than the baseline, except for the patients with a baseline eGFR < 30, no baseline hyperlipidemia, and a baseline HbA1c < 7%. However, no significant differences in eGFR were observed at 3 ($P = .95$) and 5 years ($P = .51$) postoperatively as compared with the baseline values.

Table 1: Preoperative characteristics of the study cohort ($N = 1513$).

Characteristics	Mean ± SD, N (%)
Age, years	42.7 ± 10.8
20–39	621 (41.1)
40–59	787 (52.0)
60–79	105 (6.9)
Sex	
Female	857 (56.6)
Male	656 (43.4)
Country	
Taiwan	1249 (82.6)
Japan	82 (5.4)
Korea	95 (6.3)
Hong Kong	0 (0.0)
Singapore	77 (5.1)
India	10 (0.7)
Type of surgery	
LVBG	3 (0.2)
LSG	284 (18.8)
LRYGB	406 (26.8)
LSAGB/LMGB	577 (38.1)
LAGB/LAGBP	116 (7.7)
DJBSG	114 (7.5)
Other/unspecified	13 (0.9)
Body composition	
Weight, kg	105.0 ± 25.4
Height, m	1.7 ± 0.1
BMI, kg/m^2	38.2 ± 8.0
Waist-to-hip ratio	1.0 ± 0.1
Smoking	
No	1283 (84.8)
Yes	230 (15.2)
MBP, mmHg[a]	104.9 ± 11.6
Major morbidity	
No	1360 (97.1)
Yes	40 (2.9)
Missing	113
DM-related	
Duration, years	4.6 ± 5.1
Fasting glucose, mg/dl	166.7 ± 70.2
HbA1c, %	8.3 ± 1.8
Fasting insulin, mU/l	28.4 ± 43.1
Number of oral anti-diabetic drugs	1.2 ± 1.0
Insulin therapy	
No	1261 (83.3)
Yes	252 (16.7)
C-peptide, ng/ml	4.1 ± 2.6
Laboratory measures	
Creatinine, mg/d	0.8 ± 0.4
Albumin, g/dl	4.4 ± 1.1
TC, mg/dl	207.0 ± 390.3
TG, mg/dl	223.9 ± 215.0
HDL, mg/dl	43.2 ± 12.2
LDL, mg/dl	120.4 ± 35.6
Uric acid, mg/dl	6.5 ± 2.7
ALT, U/l	52.1 ± 45.9
AST, U/l	36.8 ± 28.0
eGFR, ml/min/1.73 m^2	
≥90	1058 (69.9)
60–89	368 (24.3)
45–59	45 (3.0)
30–44	24 (1.6)
15–29	16 (1.1)
<15	2 (0.1)

TC, total cholesterol; TG, triglyceride; MBP, mean arterial pressure; LVBG, laparoscopic vertical banded gastroplasty; LSG, laparoscopic SG; LRYGB, laparoscopic Roux-en-Y gastric bypass; LAGBP, laparoscopic adjustable gastric banded plication.

[a]MBP = [SBP+2 × diastolic blood pressure (DBP)]/3.

Correlations between weight loss (%) and eGFR changes at 1 year postoperatively

Correlations of weight loss (%) and eGFR changes at 1 year postoperatively are shown in Table 7. After adjusting for age in years, sex, DM duration, baseline hypertension, baseline hyperlipidemia, and baseline HbA1c, the percentage of weight loss showed no significant correlations with eGFR changes from baseline (adjusted beta: 4.07, 95%CI: −18.31–26.44; $P = .721$).

DISCUSSION

The present study used the data from ADSS, whereas the original ADSS study did not assess renal outcomes. The results showed that eGFR values were significantly improved 1 year postoperatively, regardless of age, sex, DM duration, baseline hypertension, DM improvement after surgery, and percentage weight loss after surgery. In addition, there seems to be an overall shift toward less severe stages of CKD in the cohort at 1 year compared to baseline. However, the benefits of metabolic surgery on eGFR were not seen at 3 and 5 years postoperatively compared with baseline values. In addition, weight loss percentage at 1 year postoperatively did not correlate significantly with the eGFR improvement observed.

The initial improvement in GFR following metabolic surgery observed in the present study can be attributed to several mechanisms. First, weight loss can significantly improve renal health by reducing glomerular hyperfiltration, a common condition in obese individuals with or without diabetes that leads to increased kidney workload and potential damage [14]. Second, excess adipose tissue contributes to systemic inflammation through the release of cytokines, which can exacerbate kidney injury. Accordingly, the surgeries might also mitigate inflammatory processes, supporting overall kidney function and slowing the progression of CKD [15]. Third, the significant weight loss could reduce the strain on the cardiovascular system and lower blood pressure, thereby decreasing the risk of hypertension-related glomerular injury. Fourth, metabolic surgeries lead to better blood sugar regulation, which helps mitigate the effects of hyperglycemia-induced vascular damage, a key factor in the progression of diabetic nephropathy [9].

Despite the potential benefits at 1 year, the positive effects of metabolic surgery on eGFR appeared to be not sustained at 3 and 5 years postoperatively according to our analyses. However, due to a high dropout rate, it is relatively difficult to draw definitive conclusions from the data on the 3- and 5-year outcomes. Nevertheless, if the results are definite, several factors might explain the observed trends. For example, factors beyond immediate postoperative weight loss, such as weight regain, incomplete adherence to lifestyle changes, and aging, may play roles in determining long-term kidney function. That said, some patients may experience decreased adherence to dietary recommendations over time, which could negate the initial benefits [20]. Additionally, the kidneys may also gradually adapt to the body's new metabolic state, establishing a new homeostatic equilibrium influenced by the aging process and the natural progression of underlying renal pathologies [21]. Furthermore, changes in hormonal balances and gut microbiota induced by the surgery can affect long-term kidney function [22]. These potential confounders were not captured in the present study and, again, one should interpret the findings with caution due to the high dropout rate mentioned previously.

Metabolic bariatric surgery is known to effectively reduce weight in morbidly obese people and makes the weight loss last,

Table 2: BMI, creatinine, and eGFR of the study cohort over the follow-up period.

	N	BMI (kg/m^2)	Creatinine (mg/dl)	eGFR < 60 (%)	eGFR (ml/min/1.73 m^2)
Baseline	1513	38.2 ± 8.0	0.8 ± 0.4	87 (5.8)	104.7 ± 31.9
1 year	736	27.4 ± 5.2	0.8 ± 0.4	30 (4.1)	112.4 ± 32.0
2 year	377	27.4 ± 5.0	0.8 ± 0.6	14 (3.7)	110.4 ± 30.6
3 year	237	27.8 ± 5.0	0.8 ± 0.7	7 (3.1)	109.7 ± 28.4
4 year	129	28.5 ± 5.2	0.8 ± 0.7	4 (3.1)	106.2 ± 29.8
5 year	88	27.4 ± 5.5	0.7 ± 0.2	1 (1.1)	108.0 ± 24.2

Continuous data are presented as mean ± SD.

Table 3: Distribution of CKD stage of the study cohort at baseline and 1 year postoperatively.

Number of patients		CKD stage at 1-year post-surgery						
		Stage 1	Stage 2	Stage 3A	Stage 3B	Stage 4	Stage 5	Total (%)
Preoperative CKD stage	Stage 1	511	35	0	0	0	0	546 (74.2)
	Stage 2	72	71	5	0	0	0	148 (20.1)
	Stage 3A	1	10	5	1	0	0	17 (2.3)
	Stage 3B	1	5	6	3	2	0	17 (2.3)
	Stage 4	0	0	0	0	4	1	8 (1.1)
	Stage 5	0	0	0	0	0	0	0 (0.0)
	Total (%)	585 (79.5)	121 (16.4)	16 (2.2)	7 (1.0)	6 (0.8)	1 (0.1)	736 (100.0)

Stage 1, eGFR ≥90; stage 2, 60–80; stage 3A, 45–59; stage 3B, 30–44; stage 4, 15–29; stage 5, <15 ml/min/1.73 m^2.
Categorical variables are presented as counts (percentage).

which works better than diet, exercise, and medications. It has also been documented in clinical trials to promote remission or significant improvement in T2DM and related comorbidities [23]. Toward the goal of achieving weight loss, bariatric surgery involves surgical manipulation of the GI tract through restrictive, malabsorptive, and combined surgeries, including gastric banding, SG, distal gastric or jejunoileal bypass, biliopancreatic diversion, duodenal conversion; and Roux-en-Y gastric bypass, among others [24]. The five specific types of metabolic procedures in the present study include SG, SG plus duodenojejunal bypass (SG–DJB), one anastomotic gastric bypass, the Roux-en-Y paragastric road, and single anastomotic duodenojejunal bypass SG (SA-DJBSG).

While the renal benefits of metabolic surgery for diabetic patients are less studied, its effects on proteinuria, GFR, and hyperfiltration have been documented in obese populations, regardless of with or without DM. For instance, a study retrospectively analyzed the effects of metabolic bariatric surgery on renal function in 2247 patients, predominantly Hispanic and African American, at a community hospital in the USA. Three years postoperatively, significant improvements were observed: mean UACR decreased from 40.3 to 11.1 mg/g, mean eGFR improved from 79.4 to 87.3 ml/min, the prevalence of microalbuminuria decreased from 13.7% to 6.2%, macroalbuminuria decreased from 2.5% to 0%, and hyperfiltration prevalence decreased from 4.4% to 2.7%. These results continued to be significant even after adjusting for factors such as age, sex, race, type of surgery, and the presence of diabetes or hypertension in a multivariate regression analysis [12]. In another study focused on patients with T2DM and severe obesity, metabolic surgery (gastric bypass and SG) was associated with reduced all-cause mortality, and the surgical group experienced a 42% lower risk of nonfatal renal events compared to the control group [20]. In a systematic review conducted by Zhou *et al.*, the evidence suggests that metabolic surgery may improve albuminuria and urinary albumin-to-creatinine ratio (uACR) in patients with T2D [25]. In addition, a previous study indicated that combined metabolic surgery (gastric bypass) plus medical therapy (CSM) was superior to medical therapy alone as a means of achieving proteinuria remission at 2 years in a randomized clinical trial of microvascular outcomes after metabolic surgery for obesity and obesity [22]. Those authors indicated that improvements in BMI were not associated with improvements in metabolic and renal indices after CSM; urinary metabolites altered by CSM at 6 months showed that such changes in these urine metabolomic signatures may be associated with the renal protective effects of metabolic CSM. The exact mechanism behind the improvements in GFR following metabolic surgery is not fully understood. However, animal studies suggest that the protective effects of bariatric surgery on kidney function may be related to the inhibition of oxidative stress responses [26].

Another study relevant to the present one, conducted in an Asian cohort using the ADSS data, assessed kidney-related outcomes after metabolic bariatric surgery for obese populations [13]. That study indicated that metabolic bariatric surgery had a positive effect on renal function, with a modest but statistically significant improvement in eGFR and a reduction in

Table 4: eGFR at baseline and at 1 year postoperatively in different patient subgroups.

	N	Baseline	1 year	*P* value
Total cohort	736	106.4 ± 31.7	112.4 ± 32.0	**<.001**
Age, years				
<50	519	112.0 ± 30.8	117.3 ± 31.9	**.006**
≥50	217	93.1 ± 29.8	100.7 ± 29.1	**.007**
Sex				
Female	425	106.2 ± 30.0	112.1 ± 32.2	**.006**
Male	311	106.7 ± 33.9	112.9 ± 31.8	**.019**
DM duration				
<3 years	360	101.3 ± 33.8	108.4 ± 33.8	**.005**
≥3 years	273	112.7 ± 29.1	117.5 ± 28.4	**.048**
Missing	103			
Baseline eGFR, ml/min/1.73 m^2				
≥60	694	110.3 ± 28.0	115.8 ± 29.0	**<.001**
30–59	34	45.7 ± 8.5	63.2 ± 23.7	**<.001**
<30	8	22.1 ± 4.9	27.1 ± 12.4	.309
Baseline hypertension				
No	178	107.6 ± 31.0	116.1 ± 31.6	**.011**
Yes	528	106.2 ± 31.5	111.3 ± 30.7	**.007**
Missing	30			
Baseline hyperlipidemia				
No	275	109.5 ± 32.6	114.1 ± 32.1	.099
Yes	450	104.5 ± 31.0	111.5 ± 32.1	**.001**
Missing	11			
Baseline HbA1c, %				
<7%	170	106.7 ± 35.1	109.2 ± 33.8	.501
≥7%	561	106.3 ± 30.6	113.3 ± 31.1	**<.001**
Missing	5			
DM improved				
No	287	103.3 ± 33.1	109.6 ± 35.2	**.029**
Yes	449	108.3 ± 30.6	114.2 ± 29.7	**.004**
Weight loss, %				
≥20%	526	107.6 ± 32.5	113.2 ± 32.2	**.005**
<20%	172	105.2 ± 29.7	111.9 ± 31.6	**.042**
Missing	38			

Hypertension was defined as SBP >130 or DBP >80 mmHg.
Hyperlipidemia was defined as LDL >160 mg/dl, HDL <40 mg/dl or TG >200 mg/dl.
Improved DM was defined as HbA1c <7% at 1 year.
Weight loss was defined as percentage weight loss at 1 year compared to baseline.
Continuous data are presented as mean ± SD.
The bold values indicate statistical significance with $p < 0.05$.

Table 5: eGFR at baseline and at 3 years postoperatively in different patient subgroups.

	N	Preoperative	3 years	*P* value
Total cohort	237	109.5 ± 30.6	109.7 ± 28.4	.948
Age, years				
<50	171	113.9 ± 30.2	112.6 ± 27.6	.673
≥50	66	98.0 ± 28.7	102.0 ± 29.4	.423
Sex				
Female	134	110.4 ± 29.8	110.6 ± 30.4	.954
Male	103	108.3 ± 31.7	108.4 ± 25.6	.973
DM duration				
<3 years	103	115.0 ± 31.3	116.0 ± 25.0	.787
≥3 years	97	101.2 ± 30.2	99.5 ± 28.2	.699
Missing	37			
Baseline eGFR, ml/min/1.73 m^2				
≥60	230	111.8 ± 27.9	111.7 ± 25.9	.976
30–59	4	41.6 ± 6.4	49.1 ± 25.3	.585
<30	3	21.5 ± 4.1	31.4 ± 25.0	.535
Baseline hypertension				
No	42	111.3 ± 27.1	119.5 ± 30.9	.199
Yes	182	108.7 ± 31.8	107.2 ± 27.9	.639
Missing	13			
Baseline hyperlipidemia				
No	99	112.7 ± 31.8	112.2 ± 26.1	.902
Yes	135	106.8 ± 29.7	107.5 ± 30.1	.85
Missing	3			
Baseline HbA1c, %				
<7%	56	110.3 ± 34.9	111.9 ± 33.5	.81
≥7%	176	109.0 ± 29.4	109.1 ± 27.0	.972
Missing	5			
DM improved				
No	96	108.3 ± 34.7	107.0 ± 30.4	.784
Yes	141	110.3 ± 27.6	111.5 ± 27.0	.717
Weight loss, %				
≥20%	153	111.2 ± 32.9	111.8 ± 30.8	.878
<20%	66	108.2 ± 25.7	104.6 ± 22.8	.393
Missing	18			

Hypertension was defined as SBP >130 or DBP >80 mmHg.
Hyperlipidemia was defined as LDL >160 mg/dl, HDL <40 mg/dl or TG >200 mg/dl.
Improved DM was defined as HbA1c <7% at 3 years.
Weight loss was defined as percentage weight loss at 3 years compared to baseline.
Continuous data are presented as mean ± SD.

albuminuria at 1 year postoperatively, while indicating longer-term data are still needed to understand the persistence of this effect. According to our findings, metabolic surgery for DM population appears to have a comparable 1-year benefit on renal outcomes as observed in the general obese population.

Of note, while our current analysis employed the simplified MDRD formula for calculating eGFR, a previous study by Neff *et al*. employed three distinct formulas to compute eGFR: specifically, the MDRD, CKD Epidemiology Collaboration (CKD-EPI), and Cockcroft–Gault formulas [21]. Neff *et al*. observed an improvement in renal function not only within the first year but also throughout a 5-year follow-up period. It is worth noting that Neff *et al*. did not present results based on the Cockcroft formula. This omission might be because the Cockcroft formula incorporates body weight, which could introduce bias in the context of the study where body weight fluctuated. Furthermore, it should be noted that serum creatinine and eGFR have limitations, they are regarded as imperfect proxies for true kidney function, as they can be influenced by systemic errors stemming from factors such as muscle mass, tubular secretion, and inherent proportional bias. When an individual undergoes weight loss and experiences a reduction in lean body mass, this can result in a decrease in serum creatinine levels and an increase in eGFR. However, this can occur even when there has been no real change in the individual's true kidney function [27].

In summary, the present study provides informative longitudinal data on the effects of metabolic surgery in DM patients, particularly regarding improvements in renal function parameters. Findings suggest that the benefits of metabolic surgery are not only weight loss and blood glucose control, but also renal function.

Strengths and limitations

To the best of our knowledge, the present study is one of the few studies evaluating mid- and long-term renal functional improvements after metabolic surgery in Asian T2DM patients.

Table 6: eGFR at baseline and at 5 years postoperatively in different patient subgroups.

	N	Baseline	5 years	*P* value
Total cohort	88	110.5 ± 27.2	108.0 ± 24.2	.514
Age, years				
<50	69	113.7 ± 27.5	111.0 ± 24.2	.554
≥50	19	99.0 ± 23.6	96.7 ± 21.1	.756
Sex				
Female	59	113.2 ± 24.5	107.7 ± 21.4	.194
Male	29	105.0 ± 31.8	108.5 ± 29.4	.66
DM duration				
<3 years	36	112.6 ± 25.9	109.2 ± 20.9	.545
≥3 years	32	105.7 ± 32.0	102.7 ± 26.1	.686
Missing	20			
Baseline eGFR, ml/min/1.73 m^2				
≥60	87	111.3 ± 26.4	108.3 ± 24.1	.441
30–59	1	43.2	77.1	–
<30	0	–	–	–
Baseline hypertension				
No	30	116.2 ± 31.4	116.4 ± 27.9	.986
Yes	56	106.5 ± 24.4	103.7 ± 21.3	0.515
Missing	1			
Baseline hyperlipidemia				
No	32	107.3 ± 27.0	107.9 ± 23.1	.929
Yes	55	112.5 ± 27.7	107.5 ± 24.9	.321
Missing	1			
Baseline HbA1c, %				
<7%	21	106.6 ± 27.0	107.9 ± 28.8	.878
≥7%	66	111.6 ± 27.6	108.0 ± 22.9	.414
Missing	1			
DM improved				
No	37	101.5 ± 27.7	101.8 ± 25.1	.966
Yes	51	117.0 ± 25.2	112.4 ± 22.7	.338
Weight loss, %				
≥20%	61	112.5 ± 29.3	109.8 ± 24.7	.586
<20%	22	106.1 ± 19.0	104.4 ± 22.6	.782
Missing	5			

Hypertension was defined as SBP >130 or DBP >80 mmHg.
Hyperlipidemia was defined as LDL >160 mg/dl, HDL <40 mg/dl or TG >200 mg/dl.
Improved DM was defined as HbA1c <7% at 5 years.
Weight loss was defined as percentage weight loss at 5 years compared to baseline.
Continuous data are presented as mean ± SD.

As mentioned before, this topic is of particular interest given the rising prevalence of T2DM in Asian countries, and Asians exhibit a pronounced ethnic and genetic predisposition toward diabetes, with lower thresholds for susceptibility to environmental risk factors [28]. The main strength of the present study is its extensive cohort of Asian individuals with T2DM, combined with a relatively extended follow-up period. This enables us to investigate renal function outcomes over both the mid- and long-term in T2DM patients undergoing metabolic surgery. Nevertheless, several limitations should be noted. First, its retrospective nature, even though the data were originally collected prospectively in the ADSS, introduces the possibility of inherent biases. Second, a significant proportion of loss to follow-up (>50% at 1 year) raises concerns about the potential for bias. The continued use of relatively small sample sizes at the 3- and 5-year follow-up points could potentially result in insufficient statistical power, rendering the results less reliable. Third, albuminuria, a crucial factor in CKD diagnosis and monitoring, was not included due to a substantial amount of missing data. Furthermore, the study also did not account for certain potential confounders, such as medications like ACE inhibitors and angiotensin receptor blockers (ACEI/ARB), which can have an impact on kidney function. Last, the absence of a control group that did not undergo bariatric surgery limits our ability to comparatively assess its impact on kidney functional change.

CONCLUSIONS

Metabolic surgery performed as part of T2DM treatment leads to a significant improvement in renal function in terms of eGFR at 1 year postoperatively in Asian individuals with T2DM. Additionally, there appears an overall shift toward less severe stages of CKD in the cohort at 1 year compared to baseline. No significant improvement in GFR at 3 and 5 years compared to baseline was observed; however, a definitive conclusion may not be drawn due to the high dropout rate. Further studies are warranted to confirm these findings and to include other renal functional parameters such as albuminuria.

Table 7: Correlation of weight loss and other factors with eGFR change at 1 year postoperatively.

	eGFR change (vs. preoperative)			
Variables	Crude beta (95% CI)	P	Adjusted beta (95% CI)[a]	P
Weight loss, %	2.55 (−16.76, 21.86)	.796	4.07 (−18.31, 26.44)	.721
Age, years	**0.15 (0.002, 0.30)**	**.047**	0.17 (−0.02, 0.35)	.076
Sex				
Female	ref		ref	
Male	0.35 (−2.99, 3.70)	.835	2.08 (−1.59, 5.75)	.266
DM duration				
<3 y	ref		ref	
≥3 y	−2.29 (−5.84, 1.25)	.204	−1.41 (−5.42, 2.60)	.489
Baseline hypertension				
No	ref		ref	
Yes	−3.36 (−7.28, 0.55)	.092	−3.48 (−7.77, 0.80)	.111
Baseline hyperlipidemia				
No	ref		ref	
Yes	2.37 (−1.11, 5.86)	.182	0.23 (−3.64, 4.11)	.906
Baseline HbA1c				
<7%	ref		ref	
≥7%	**−4.48 (−8.33, −0.63)**	**.023**	−3.65 (−8.42, 1.12)	.134

Continuous data are presented as mean ± SD. Categorical variables are presented as counts (percentage).

P < .05 are shown in bold.

[a]Adjusted for age in years, sex, DM duration, baseline hypertension, baseline hyperlipidemia, baseline HbA1c.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

Y.-M.H., C.-Y.L., and W.W. developed the concept and design; W.-J.L., K.Y.H., and K.K. provided administrative support; A.K.S.C. and M.-H.L. provided study materials or patients; S.C., K.-H.W., and T.-C.S. collected and assembled data; K.-T.L., D.L., M.L., Y.-H.S., and H.-H.Ch. carried out data analysis and interpretation; and all authors; were involved in the writing and the approval of the final paper.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

None declared.

ETHICAL APPROVAL

The study protocol was reviewed and approved by the Institutional Review Boards of the respective institutions (IRB No MSIRB2015002, CRE 2010.109, YCR18027, and N201810050). Because patient data were deidentified in this retrospective study, the IRB waived signed informed consent of included patients.

REFERENCES

1. Roden M, Shulman GI. The integrative biology of type 2 diabetes. *Nature* 2019;**576**:51–60. https://doi.org/10.1038/s41586-019-1797-8
2. Bima AIH, Elsamanoudy AZ, Albaqami WF *et al.* Integrative system biology and mathematical modeling of genetic networks identifies shared biomarkers for obesity and diabetes. *Math Biosci Eng* 2022;**19**:2310–29. https://doi.org/10.3934/mbe.2022107
3. Sun H, Saeedi P, Karuranga S *et al.* IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract* 2022;**183**:109119. https://doi.org/10.1016/j.diabres.2021.109119
4. Ma RC, Chan JC. Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States. *Ann N Y Acad Sci* 2013;**1281**:64–91. https://doi.org/10.1111/nyas.12098
5. Shen SC, Lee WJ, Kasama K *et al.* Efficacy of different procedures of metabolic surgery for type 2 diabetes in Asia: a multinational and multicenter exploratory study. *Obes Surg* 2021;**31**:2153–60. https://doi.org/10.1007/s11695-021-05239-7
6. Syn NL, Cummings DE, Wang LZ *et al.* Association of metabolic-bariatric surgery with long-term survival in adults with and without diabetes: a one-stage meta-analysis of matched cohort and prospective controlled studies with 174 772 participants. *Lancet* 2021;**397**:1830–41. https://doi.org/10.1016/S0140-6736(21)00591-2
7. Rao WS, Shan CX, Zhang W *et al.* A meta-analysis of short-term outcomes of patients with type 2 diabetes mellitus and BMI ≤35 kg/m^2 undergoing Roux-en-Y gastric bypass. *World J Surg* 2015;**39**:223–30. https://doi.org/10.1007/s00268-014-2751-4
8. Rubino F, Nathan DM, Eckel RH *et al.* Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement

by International Diabetes Organizations. *Obes Surg* 2017;**27**: 2–21. https://doi.org/10.1007/s11695-016-2457-9

9. Aminian A, Zajichek A, Arterburn DE *et al*. Association of metabolic surgery with major adverse cardiovascular outcomes in patients with type 2 diabetes and obesity. *JAMA* 2019;**322**:1271–82. https://doi.org/10.1001/jama.2019.14231
10. Adler AI, Stevens RJ, Manley SE *et al*. Development and progression of nephropathy in type 2 diabetes: the United Kingdom prospective Diabetes Study (UKPDS 64). *Kidney Int* 2003;**63**:225–32. https://doi.org/10.1046/j.1523-1755.2003.00712.x
11. Martin WP, White J, López-Hernández FJ *et al*. Metabolic surgery to treat obesity in diabetic kidney disease, chronic kidney disease, and end-stage kidney disease; what are the unanswered questions? *Front Endocrinol* 2020;**11**:289. https://doi.org/10.3389/fendo.2020.00289
12. Saeed K, Ahmed L, Suman P *et al*. Bariatric surgery improves renal function: a large inner-city population outcome study. *Obes Surg* 2021;**31**:260–6. https://doi.org/10.1007/s11695-020-04909-2
13. Wee Z, Ganguly S, Tham KW *et al*. Renal outcomes 1 year after metabolic bariatric surgery in a multi-ethnic Asian cohort. *Obes Surg* 2021;**31**:5358–66. https://doi.org/10.1007/s11695-021-05732-z
14. Chang AR, Grams ME, Navaneethan SD. Bariatric surgery and kidney-related outcomes. *Kidney Int Rep* 2017;**2**:261–70. https://doi.org/10.1016/j.ekir.2017.01.010
15. Huang H, Lu J, Dai X *et al*. Improvement of renal function after bariatric surgery: a systematic review and meta-analysis. *Obes Surg* 2021;**31**:4470–84. https://doi.org/10.1007/s11695-021-05630-4
16. Lee WJ, Hur KY, Lakadawala M *et al*. Predicting success of metabolic surgery: age, body mass index, C-peptide, and duration score. *Surg Obes Relat Dis* 2013;**9**:379–84. https://doi.org/10.1016/j.soard.2012.07.015
17. Shen Y, Cai R, Sun J *et al*. Diabetes mellitus as a risk factor for incident chronic kidney disease and end-stage renal disease in women compared with men: a systematic review and meta-analysis. *Endocrine* 2017;**55**:66–76. https://doi.org/10.1007/s12020-016-1014-6
18. Favre G, Schiavo L, Lemoine S *et al*. Longitudinal assessment of renal function in native kidney after bariatric surgery. *Surg Obes Relat Dis* 2018;**14**:1411–8. https://doi.org/10.1016/j.soard.2018.05.013
19. Holcomb CN, Goss LE, Almehmi A *et al*. Bariatric surgery is associated with renal function improvement. *Surg Endosc* 2018;**32**:276–81. https://doi.org/10.1007/s00464-017-5674-y
20. Doumouras AG, Lee Y, Paterson JM *et al*. Association between bariatric surgery and major adverse diabetes outcomes in patients with diabetes and obesity. *JAMA Netw Open* 2021;**4**:e216820. https://doi.org/10.1001/jamanetworkopen.2021.6820
21. Neff KJ, Baud G, Raverdy V *et al*. Renal function and remission of hypertension after bariatric surgery: a 5-year prospective cohort study. *Obes Surg* 2017;**27**:613–9. https://doi.org/10.1007/s11695-016-2333-7
22. Martin WP, Malmodin D, Pedersen A *et al*. Urinary metabolomic changes accompanying albuminuria remission following gastric bypass surgery for type 2 diabetic kidney disease. *Metabolites* 2022;**12**:139. https://doi.org/10.3390/metabo12020139
23. Gentileschi P, Bianciardi E, Benavoli D *et al*. Metabolic surgery for type II diabetes: an update. *Acta Diabetol* 2021;**58**:1153–9. https://doi.org/10.1007/s00592-021-01722-w
24. Chalopin S, Betry C, Coumes S *et al*. Benefits and risks of bariatric surgery in patients with bipolar disorders. *Surg Obes Relat Dis* 2020;**16**:798–805. https://doi.org/10.1016/j.soard.2020.02.010
25. Zhou X, Li L, Kwong JS *et al*. Impact of bariatric surgery on renal functions in patients with type 2 diabetes: systematic review of randomized trials and observational studies. *Surg Obes Relat Dis* 2016;**12**:1873–82. https://doi.org/10.1016/j.soard.2016.05.003
26. Jiang HW, Zhou Y, Zhou PY *et al*. Protective effects of bariatric surgery on kidney functions by inhibiting oxidative stress responses through activating pparα in rats with diabetes. *Front Physiol* 2021;**12**:662666. https://doi.org/10.3389/fphys.2021.662666
27. Nankivell BJ, Nankivell LFJ, Elder GJ *et al*. How unmeasured muscle mass affects estimated GFR and diagnostic inaccuracy. *Eclin Med* 2020;**29-30**:100662. https://doi.org/10.1016/j.eclinm.2020.100662
28. Zuo H, Shi Z, Hussain A. Prevalence, trends and risk factors for the diabetes epidemic in China: a systematic review and meta-analysis. *Diabetes Res Clin Pract* 2014;**104**:63–72. https://doi.org/10.1016/j.diabres.2014.01.002

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