The impact of bariatric surgery on estimated glomerular filtration rate in patients with type 2 diabetes

Mirajkar, Nikhil; Bellary, Srikanth; Ahmed, Mohamed; Singhal, Rishi; Daskalakis, Markos; Tahrani, Abd A

DOI:
10.1016/j.soard.2016.02.024

Abstract

Background: Diabetes mellitus (DM) is the ~~commonest~~ most common cause of end-stage renal disease (ESRD). ESRD is associated with increased morbidity and mortality. Our primary aim was to assess the impact of bariatric surgery on ~~renal function~~estimated glomerular filtration rate (eGFR) in patients with Type 2 DM (T2DM). Our secondary aim was to compare the impact of bariatric surgery vs. routine care on ~~renal function~~eGFR in patients with T2DM.

Methods: A retrospective cohort analysis of adults with T2DM who underwent bariatric surgery at single center in the UK between January 2005 and December 2012. ~~Renal function (measured by estimated glomerular filtration rate (eGFR))~~Data regarding eGFR was obtained from electronic patients records. eGFR was calculated using the MDRD (Modification of Diet in Renal Disease) formula. Data regarding patients with T2DM who did not undergo bariatric surgery ("routine care") were obtained from patients attending the diabetes clinic at the same centre 2009-2011.

Results: 163 patients were included (mean age 48.5±8.8 years, baseline Body Mass Index (BMI) (50.8±9.1kg/m^2) and were followed for 3.0±2.3 years. Bariatric surgery resulted in an improvement in eGFR (median (IQR) 86.0 (73.0-100.0) vs. 92.0 (77.0-101.0) ml/min/1.73m^2 for baseline vs. follow-up respectively; p= 0.003) particularly in patients with baseline eGFR ≤~~<~~60 ml/min/1.73m^2 (48.0 (42.0-57.0) vs. 61.0 (55.0-63.0) ml/min/1.73m^2; p= 0.004). After adjusting for baseline eGFR, glycated hemoglobin (A1C) (HbA1c), BMI, age and gender, bariatric surgery was associated with higher study-end eGFR compared to routine care (B=7.787, p=<0.001)

Conclusion: Bariatric surgery results in significant improvements in ~~renal function~~eGFR in patients with T2DM, particularly in those with an eGFR ≤~~<~~60 ml/min/1.73m^2, while routine care was associated with a decline in eGFR.

Introduction

Chronic kidney disease (CKD) secondary to diabetes is the most common cause of end-stage renal disease (ESRD) and is associated with increased morbidity and mortality [1;2]. About 20–40% of patients with microalbuminuria can progress to overt proteinuria of which 20% will have progressed to ESRD within 20 years [1]. CKD progression to ESRD requiring renal replacement therapy (RRT) is variable and depends on multiple modifiable and non-modifiable factors such as obesity, blood pressure (BP), metabolic control, gender and ethnicity [3;4].

Glycaemic and BP control and the use of renin–angiotensin–aldosterone system (RAAS) inhibitors are the mainstay of treatment in order to slow down the decline in renal function and the progression to ESRD; but despite better metabolic control in patients with Type 2 diabetes mellitus (T2DM), ESRD remains very common [5].

Obesity, which is very common in patients with T2DM, is also a modifiable risk factor in the development of CKD [6-8]. The mechanisms linking obesity to CKD are complex and multifactorial including hypertension, activation of the sympathetic nervous system, activation of the RAAS, increased inflammation, low adiponectin, insulin resistance, obstructive sleep apnea (OSA) and endothelial dysfunction amongst others [8-11].

Meta-regression analysis from 522 patients across 13 trials showed that independent of decline in mean arterial pressure, each 1 kg weight loss was associated with 110 mg (95% CI 60-160 mg, $p < 0.001$) decrease in proteinuria and 1.1 mg (95% CI 0.5-2.4 mg, $P = 0.011$) decrease in microalbuminuria [12]; potentially suggesting an important role for weight loss in the management of CKD and emphasizing the importance of obesity in the pathogenesis of CKD.

Bariatric surgery is the most effective treatment for obesity that results in sustained long term weight loss [13]. Several randomized and non-randomized clinical trials showed that bariatric surgery was superior to intensive medical management in patients with T2DM particularly in regards metabolic parameters including hyperglycaemia, weight, BP, hypertriglyceridemia and low HDL [14-18]. Diabetes remission rates following bariatric surgery were 30-90% depending on the definition of the remission used, length of follow up, the type of bariatric surgery and diabetes duration amongst other factors [14;16;17;19;20].

Hence, due to its impact on multiple CKD and cardiovascular disease risk factors it would be expected that bariatric surgery could have a favourable impact on renal function in patients with T2DM. On the other hand, bariatric surgery might have no impact on renal function in the short-medium term due the effect of metabolic memory resulting in sustained vascular dysfunction despite improvements in metabolic control and weight loss [21]. Bariatric surgery, particularly Roux-en-Y gastric bypass (RYGB), might even have a harmful effect on the kidneys due to possibility of chronic hyperoxaluria resulting in further insult to kidneys that are already damaged by diabetes[22].

The primary aim of this study was to assess the impact of bariatric surgery on ~~renal function~~ estimated glomerular filtration rate (eGFR) in patients with T2DM. A secondary aim was to compare the impact of bariatric surgery vs. routine care in patients with T2DM.

Methods

We conducted a retrospective cohort analysis of adult patients (≥ 18 years old) with T2DM who underwent bariatric surgery at our centre in the UK between January 2005 and December 2012. Data regarding patients who had bariatric surgery and their diabetes status

were obtained from a prospectively maintained bariatric surgery database which is kept up to date by the weight management team. ~~Renal function (as measured by estimated glomerular filtration rate (eGFR))~~Data regarding eGFR was obtained from the electronic patients records. Baseline eGFR was defined as the latest eGFR available within 1 month preceding surgery. Follow-up eGFR was the latest available on our hospital electronic system post-surgery. Patients with no baseline or follow-up eGFR were excluded from analysis. eGFR was calculated using the MDRD (Modification of Diet in Renal Disease) formula. eGFR ≥ 120 ~~mls~~ml/min/1.73m^2 was considered to be consistent with hyperfiltration as in previous studies [23-25].

Data regarding patients with T2DM who did not undergo bariatric surgery ("routine care") were obtained from another prospective study assessing the pathogenesis of microvascular complications in patients with T2DM. The comparator prospective study included adults with T2DM and excluded patients with end-stage renal disease. Patients in this group were recruited from the diabetes clinic at the same centre in which the bariatric surgery was performed 2009-2011.

The comparator "routine care" group data was collected as part of a project that was approved by the Warwickshire Research Ethics Committee (REC number 08/H1211/145). The data regarding patients who underwent bariatric surgery and their eGFR were collected during routine clinical care and as part of health service evaluation assessing the outcomes of bariatric surgery at our centre, and hence ethical approval was not required.

Data analysis was performed using SPSS 22.0 software (SPSS Inc, Chicago, USA). Data was presented as frequencies or mean (SD) ~~or median (IQR) depending on data distribution~~. Independent continuous variables were compared using the Student's t-test. Paired t-test

was used to compare pre- and post- surgical parameters. Non-parametric tests were used if the data was not normally distributed. ~~Pearson or Spearman tests (depending on data distribution) were used to correlate changes in eGFR with changes in metabolic parameters.~~ Categorical variables were compared using the Chi-squared test. Multiple linear regression models were used to assess predictors of study-end eGFR in patients who underwent bariatric surgery and to assess the relationship between bariatric surgery vs. routine care and study-end eGFR. Predictors inserted in the models based on factors that are related to the outcome measure. The linear regression models were assessed for multicollinearity, homoscedasticity and influential cases and the residuals were assessed for normality. A sub-group analysis based on the type of the bariatric surgical procedure and baseline eGFR ~~assessing the impact of bariatric surgery on eGFR in patients with eGFR < 60 mls~~ml~~/min/1.73m^2~~ was also performed. Changes to eGFR were also compared between patients with T2DM who received bariatric surgery vs. routine care ~~in a subgroup of patients~~. A p value < 0.05 was considered significant.

Results

Between January 2005 and December 2012, 565 patients with T2DM underwent bariatric surgery at our centre. Out of the 565 patients, only 163 had a baseline and follow-up eGFR measurements. There were no difference in age, gender, baseline weight or baseline BMI between those who were included and those were excluded from the analysis.

Of the 163 patients who underwent bariatric surgery, 66.9% (n=109) were women, 60.7% (n=99) received laparoscopic adjustable gastric banding (LAGB), 28.9~~8~~% (n=47) Roux-en-Y gastric bypass (RYGB), 5.5% (n=9) laparoscopic sleeve gastrectomy (LSG) and 4.9% (n=8) had the type of surgery unrecorded in the database. The mean patient age at the time of

bariatric surgery was 48.5±8.8 years (range 26-74 years). Patients were followed up for a median of 2 years post surgery (range 1.3-9.9 years, mean ± SD 3.04±2.3 years).

Bariatric surgery resulted in significant improvements in HbA1c (60.5±18.7 mmol/mol vs. 52.6±18.2mmol/mol; p <0.001) and BMI (50.8±9.1 kg/m^2 vs. 40.4±9.2 kg/m^2; p <0.001) (data available on baseline and study-end HbA1c and BMI in 157 and 152 patients respectively).

Bariatric surgery and CKD

Bariatric surgery resulted in a significant improvement in eGFR particularly in patients with baseline eGFR ≤~~<~~60 ml/min/1.73m^2 (mainly indicating CKD stage 3) (n=15/163, 9.2%) (**Table 1**)

The change in eGFR (defined as study end – baseline values) was greater in patients with baseline eGFR ≤~~<~~ 60 ml/min/1.73m^2 vs. those with baseline eGFR ~~≥~~> 60 ml/min/1.73m^2 (14.0 (4.0-20.0) ml/min/1.73m^2 vs. 4.0 (-6.8-10.0) ml/min/1.73m^2; p=0.009 using the Mann-Whitney U test).

~~The change in eGFR was greater in patients who had RYGB compared to LAGB and VSG (9.0 (1.0-14.0) mls/min/1.73m^2 vs. 4.0 (-8.0-9.0) mls/min/1.73m^2 vs. 2.0 (-9.5-16.0) mls/min/1.73m^2 for RYGB, LAGB and VSG respectively; p= 0.027).~~ There were no differences in eGFR change between men and women (p=0.95).

Baseline eGFR (B=0.65, p<0.001), follow-up duration (B=-1.6, p=0.002) and baseline HbA1c (B= -0.14, p=0.03) were independent predictors of study-end eGFR after adjustment for age, baseline eGFR, baseline HbA1c, baseline BMI, HbA1c change, BMI change, and follow-up duration (R^2 for the model 0.55).

Subgroup analysis based on baseline eGFR and bariatric surgical procedure (**Table 2**) showed that LAGB and RYGB improved eGFR in patients with baseline eGFR ≤ 60 ml/min/1.73m^2 and 60 to < 90 ml/min/1.73m^2. In patients with eGFR 90 to < 120 ml/min/1.73m^2 LAGB resulted in improvements in eGFR while RYGB had no impact on eGFR. In patients with hyperfiltration (eGFR ≥ 120 ml/min/1.73m^2) and received LAGB eGFR improved (Table 2).

Bariatric surgery vs. routine care: Uni- and multi- variable analysis

Patients in the routine care group were older (p<0.001) and had higher baseline HbA1c compared (p<0.001) to the bariatric surgery group; while the surgical group were heavier (p<0.001) and had on average slightly longer follow-up (p=0.02) (**Table ~~2~~3**). Patients in the routine care group had a mean±SD blood pressure of 130.0 ± 17.3/78.2 ± 10.4 mmHg. The routine care group were intensively treated with glucose and blood pressure lowering agents including: insulin in 53.3% (n=120), oral glucose lowering agents 92.4% (n=208), renin-angiotensin-aldosterone system inhibitors 69.8% (n=157) and 80% (n=180) received one or more antihypertensive. The median number of antihypertensives used per patient in the routine care was 2 (IQR 1-2).

The baseline eGFR was similar between groups but the study-end eGFR and the eGFR change were greater in the bariatric surgery group compared to the routine care group (**Table ~~3~~4**). In the bariatric surgery group eGFR increased while in the routine care group eGFR decreased during the follow-up (p<0.001) (**Table 4**). This difference was particularly evident in patients with baseline eGFR ≤ 60 ml/min/1.73m^2 (p<0.001) (**Table 4**).

After adjustment for baseline differences, bariatric surgery was independently and significantly (p<0.001) associated with higher study-end eGFR **(Table 5**). Other independent predictors of study-end eGFR included baseline eGFR, age and follow-up duration (**Table 5**).

Discussion

This study shows that bariatric surgery resulted in significant improvements in ~~renal functione~~GFR in morbidly obese patients with T2DM particularly in those with an eGFR ≤~~<~~60 ~~mls~~ml/min/1.73m^2. Furthermore, while bariatric surgery improved ~~renal functione~~GFR, the ~~renal functione~~GFR continued to decline gradually in a comparative group of patients with T2DM who did not have bariatric surgery. Post-surgery eGFR was not related to post surgical changes in BMI or HbA1c but was related to baseline eGFR, baseline HbA1c and age. The favourable impact of bariatric surgery on ~~renal functione~~GFR compared to routine care was independent of the between-group differences and occurred despite the slightly longer follow-up duration in the surgical group.

Despite improvements in the management of cardiovascular disease risk factors and glycaemic measures in patients with diabetes, ESRD remains very common and the decline in ESRD was far less than that observed in relation to cardiovascular disease and other diabetes-related complications in the US over 2 decades [5]. This in part could be due to the lack of effective weight loss strategies in patients with T2DM as most of the glucose lowering agents are either weight neutral or cause weight gain except GLP-1 receptor agonists and SGLT-2 inhibitors which were introduced more recently in 2005 and 2013 respectively [26;27].

Obesity, which is very common in patients with T2DM, is known to be a risk factor for ESRD via multifactorial mechanisms with weight loss having been shown to have a favourable impact on CKD and proteinuria [6-12]. A recent systematic review showed that weight loss following lifestyle changes, pharmacotherapy or bariatric surgery was generally associated with either improvements or stability in renal function and markers of CKD (such as

albuminuria or proteinuria) [28]. There are however conflicting results and the data regarding bariatric surgery was from uncontrolled and non-randomised studies of duration of 1 year or less [28;29]. More recent studies have shown that eGFR was reduced in patients with hyperfiltration and improved in patients with impaired renal function post RYGB and LSG [29-31].

Studies regarding the impact of bariatric surgery on eGFR in patients with diabetes are limited and there are no randomised controlled trials reported [8;29;32]. In a study of 50 patients with newly diagnosed T2DM, biliary pancreatic diversion was associated with improvements in eGFR compared to a decline in eGFR in the comparator arm over 10 years [33]. Another study of 30 patients with T2DM who had either LAGB, LSG or RYGB showed that surgery resulted in reductions in cystatin C levels suggesting improvements in renal function [34]. In another study that included a subgroup of patients with T2DM, RYGB resulted in improvements in glomerular hyperfiltration 12 months post surgery [35].

The impact of bariatric surgery on ~~renal function~~eGFR could be difficult to elucidate as on one hand bariatric surgery results in sustained and significant improvements in many CKD risk factors (such as weight, glycaemia, BP, inflammation etc.) [14-18]; while on the other hand the effects of the metabolic memory resulting in sustained vascular dysfunction despite improvements in glycaemic control might blunt the potential beneficial effects of bariatric surgery on ~~renal function~~the kidneys [21]. This was supported by a recent study showing that while bariatric surgery might have a favourable impact on diabetic retinopathy in patients with T2DM, sight threatening retinopathy might develop for the first time after bariatric surgery [36]. The findings of our current study show similar results in that although bariatric surgery had a beneficial effect on ~~renal function~~eGFR in patients with T2DM; baseline HbA1c

remained an independent predictor of the study-end eGFR regardless of the improvements in HbA1c that occurred post surgery.

One of the main factors regarding the difficulty in assessing the impact of bariatric surgery on renal function is the methods used to ~~assess renal function~~calculated eGFR. Creatinine-based eGFR is widely used in routine care as it is readily available and can be used in large epidemiological studies; however, there have been concerns that eGFR could be misleading in patients post bariatric surgery due to the loss of muscle mass resulting in a reduction in the supply of creatinine. In fact, creatinine-based eGFR is not validated in obese individuals and as obese individuals have higher muscle mass creatinine-based eGFR may underestimate renal function is such population [37]. Recent studies demonstrated that c~~C~~ystatin-C based eGFR was more closely related to the measured GFR than creatinine based eGFR post bariatric surgery, which is not surprising considering that cystatin-C may not be as closely related to muscle mass as creatinine and is not affected by dietary intake; [37]. ~~Indeed~~ ~~studies using measured rather than estimated GFR showed that bariatric surgery results in renal function decline and~~ ~~a~~A recent study in which measured and estimated GFR were performed in the same population 6 and 12 months following bariatric surgery showed a drop in measured GFR which was not detected by eGFR [38]. However, despite the limitations of using creatinine-based eGFR a recent study showed that calculating eGFR based on creatinine and cystatin-C combined using the CKD-EPI was superior to calculating eGFR based on either creatinine or cys~~c~~tatin-C alone when compared to measured GFR; but in this study the surgery type was not defined and almost all included patients had normal renal function at baseline[37].

In our study we have used estimated and not measured GFR and in the absence of ~~a~~ measured muscle mass before and after surgery in this study we cannot completely rule out the impact of reduction in creatinine generation on our results. However, there are several factors to suggest that loss of muscle mass do not explain our findings. The loss of muscle mass following bariatric surgery is mainly reported following biliary pancreatic diversion, RYGB and LSG while several studies showed little to no loss of muscle mass following LAGB[39-41], which constitute the majority of the patients in this study. In addition, in this study the impact of LAGB on eGFR was similar to the impact of RYGB, particularly in patients with eGFR < 90 ml/min/1.73m^2 (Table 2), despite the predicted differences in muscle mass loss following LAGB and RYGB. A recent study showed that changes in muscle mass at three months were predicted by fat mass loss and changes in glycaemia, whereas change in glycaemia was the only 12-month determinant associated with muscle mass changes following RYGB or LSG [42]. Our results show that the changes in eGFR were independent of changes in BMI and changes in HbA1c ~~suggesting that the impact of bariatric surgery in our study may not totally reflect the changes in muscle mass~~. Furthermore, the time course of muscle mass loss suggest that muscle mass loss recovers, at least partially, at 12 months compared to 3 months post-surgery[42]; considering that the average follow-up duration in this study is 3.04 years and the range is 1.3-9.9 years, this would suggest that the impact of muscle mass loss might have been lessened further with the longer follow-up. Finally, with loss of creatinine supplies due to muscle mass loss after surgery it would be expected that eGFR would increase regardless of baseline eGFR, but the results in Table 2 show that eGFR has indeed dropped in patients who received LAGB with baseline eGFR ≥ 90 ml/min/1.73m^2 and that RYGB and LSG did not result in eGFR changes in patients with baseline eGFR between 90 and < 120 ml/min/1.73m^2. All the above factors suggest that loss of creatinine

generation, caused by muscle mass loss post bariatric surgery, does not fully explain the findings of this study.

The mechanisms underpinning the observed impact of bariatric surgery on ~~renal function~~eGFR are unclear. Changes in BMI and HbA1c did not predict ~~renal function~~eGFR changes in this study but improvements in other unmeasured CKD risk factors such as inflammation, sympathetic tone, the RAAS, OSA and endothelial function might explain the favourable impact of bariatric surgery on eGFR compared to routine care. ~~The higher improvements in eGFR in the RYGB group compared to the LSG and LAGB groups suggest that neuro-hormonal mechanisms might play a role in the impact of bariatric surgery on eGFR.~~

Our study does however have several strengths. Our study has a longer follow up and larger sample size than previous studies that assessed the relationship between CKD and bariatric surgery in patients with T2DM (except the study that used biliary pancreatic diversion) [8;29;32-35]. In addition we have compared the changes in ~~renal function~~eGFR in patients who received bariatric surgery with patients receiving their ~~medical treatment~~routine care for T2DM in the same center and hence received the same standards of care. LAGB was the predominant surgical procedure in this study and most of the literature examining the impact of bariatric surgery on renal function in T2DM has so far focused on RYGB or LSG[8;29;32-35]. On the other hand, our study has several limitations. Our data did not include BP which has an important impact on renal function[22]. However, the routine care cohort in this study had very good BP control ~~(mean 130/78 mmHg)~~ which should have minimised this effect. The observational nature of the study means that some confounders may not have been accounted for at baseline. There were also several differences in the routine care

group compared to the bariatric surgery group; however despite adjustment for these differences bariatric surgery remained an independent predictor of a higher study-end eGFR compared to routine care. Another limitation is the number of patients who were not included in the analysis due to missing data; although we could not detect any significant differences between patients who were included and those who were excluded from the analysis, we cannot rule out differences in other variables that were not measured or were not available on our electronic records.

In conclusion, bariatric surgery is associated with improvements in ~~renal function~~eGFR in patients with T2DM, particularly in those with impaired pre-operative renal function. Compared to routine care, bariatric surgery was associated with better study-end ~~renal function~~eGFR. Future studies using more assessments of renal function that are not dependent on muscle mass (such as c~~C~~ystatin-C based eGFR or using other methods such as free light chains), and longer follow up are needed to assess whether bariatric surgery can prevent or delay the development of ESRD in patients with T2DM. Studies including a larger proportion of patients with T2DM and impaired renal function are also needed to clarify whether bariatric surgery can improve renal function in this population. Whether the impact of bariatric surgery varies between different surgical approaches also requires additional investigation.

Reference List

(1) Leiter LA. The prevention of diabetic microvascular complications of diabetes: Is there a role for lipid lowering? *Diabetes Research and Clinical Practice* 2005; 68(Supplement 2):S3-S14.

(2) Bakris GL. Recognition, Pathogenesis, and Treatment of Different Stages of Nephropathy in Patients With Type 2 Diabetes Mellitus. *Mayo Clinic Proceedings* 2011; 86(5):444-456.

(3) Dronavalli S, Duka I, Bakris GL. The pathogenesis of diabetic nephropathy. *Nat Clin Pract End Met* 2008; 4(8):444-452.

(4) Afghahi H, Cederholm J, Eliasson B et al. Risk factors for the development of albuminuria and renal impairment in type 2 diabetes–the Swedish National Diabetes Register (NDR). *Nephrology Dialysis Transplantation* 2011; 26(4):1236-1243.

(5) Gregg EW, Li Y, Wang J et al. Changes in Diabetes-Related Complications in the United States, 1990–2010. *N Engl J Med* 2014; 370(16):1514-1523.

(6) MacLaughlin HL, Hall WL, Sanders TA, Macdougall IC. Risk for chronic kidney disease increases with obesity: Health Survey for England 2010. *Public health nutrition* 2015;1-6.

(7) Hsu Cy, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body Mass Index and Risk for End-Stage Renal Disease. *Annals of Internal Medicine* 2006; 144(1):21-28.

(8) Rao B, Bhattacharya A, Agrawal V. Renal outcomes of bariatric surgery in obese adults with diabetic kidney disease. *J Nephrol* 2014; 27(4):361-370.

(9) Wickman C, Kramer H. Obesity and Kidney Disease: Potential Mechanisms. *Seminars in Nephrology* 33(1):14-22.

(10) Tahrani AA, Ali A, Raymond NT et al. Obstructive Sleep Apnea and Diabetic Nephropathy: A cohort study. *Diabetes Care* 2013; 36(11):3718-3725.

(11) Tahrani AA, Dubb K, Raymond NT et al. Cardiac autonomic neuropathy predicts renal function decline in patients with type 2 diabetes: a cohort study. *Diabetologia* 2014; 57(6):1249-1256.

(12) Afshinnia F, Wilt TJ, Duval S, Esmaeili A, Ibrahim HN. Weight loss and proteinuria: systematic review of clinical trials and comparative cohorts. *Nephrology Dialysis Transplantation* 2010; 25(4):1173-1183.

(13) Sjöström L, Peltonen M, Jacobson P. Bariatric surgery and long-term cardiovascular events. *JAMA* 2012; 307(1):56-65.

(14) Dixon JB, O'Brien PE, Playfair J. Adjustable gastric banding and conventional therapy for type 2 diabetes: A randomized controlled trial. *JAMA* 2008; 299(3):316-323.

(15) Ikramuddin S, Korner J, Lee W. Roux-en-y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: The diabetes surgery study randomized clinical trial. *JAMA* 2013; 309(21):2240-2249.

(16) Schauer PR, Kashyap SR, Wolski K et al. Bariatric Surgery versus Intensive Medical Therapy in Obese Patients with Diabetes. *N Engl J Med* 2012; 366(17):1567-1576.

(17) Schauer PR, Bhatt DL, Kirwan JP et al. Bariatric Surgery versus Intensive Medical Therapy for Diabetes 3-Year Outcomes. *N Engl J Med* 2014; 370(21):2002-2013.

(18) Sjöström L, Lindroos AK, Peltonen M et al. Lifestyle, Diabetes, and Cardiovascular Risk Factors 10 Years after Bariatric Surgery. *N Engl J Med* 2004; 351(26):2683-2693.

(19) Mas-Lorenzo A, Benaiges D, Flores-Le-Roux JA et al. Impact of Different Criteria on Type 2 Diabetes Remission Rate After Bariatric Surgery. *OBES SURG* 2014; 24(11):1881-1887.

(20) Sjöström L, Peltonen M, Jacobson P. Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. *JAMA* 2014; 311(22):2297-2304.

(21) Reddy M, Zhang E, Natarajan R. Epigenetic mechanisms in diabetic complications and metabolic memory. *Diabetologia* 2014;1-13.

(22) Jackson S, le Roux C, Docherty N. Bariatric Surgery and Microvascular Complications of Type 2 Diabetes Mellitus. *Curr Atheroscler Rep* 2014; 16(11):1-9.

(23) Bjornstad P, Cherney DZ, Snell-Bergeon JK et al. Rapid GFR decline is associated with renal hyperfiltration and impaired GFR in adults with Type 1 diabetes. *Nephrology Dialysis Transplantation* 2015; 30(10):1706-1711.

(24) Hasslacher C, Kulozik F. Influence of renal function on serum concentration of 1,5-anhydroglucitol in type 2 diabetic patients in CKD stages I-III: A comparative study with HbA1c and glycated albumin. *J Diabetes* 2015;n/a.

(25) Oh SW, Han KH, Han SY. Associations between Renal Hyperfiltration and Serum Alkaline Phosphatase. *PLoS ONE* 2015; 10(4):e0122921.

(26) Tahrani AA, Bailey CJ, Del Prato S, Barnett AH. Management of type 2 diabetes: new and future developments in treatment. *The Lancet* 2011; 378(9786):182-197.

(27) Tahrani AA, Barnett AH, Bailey CJ. SGLT inhibitors in management of diabetes. *The Lancet Diabetes & Endocrinology* 2013; 1(2):140-151.

(28) Bolignano D, Zoccali C. Effects of weight loss on renal function in obese CKD patients: a systematic review. *Nephrology Dialysis Transplantation* 2013; 28(suppl 4):iv82-iv98.

(29) Neff KJ, Frankel AH, Tam FW, Sadlier DM, Godson C, le Roux CW. The effect of bariatric surgery on renal function and disease: a focus on outcomes and inflammation. *Nephrology Dialysis Transplantation* 2013; 28(suppl 4):iv73-iv82.

(30) Hou CC, Shyu RS, Lee WJ, Ser KH, Lee YC, Chen SC. Improved renal function 12 months after bariatric surgery. *Surgery for Obesity and Related Diseases* 2013; 9(2):202-206.

(31) Reid TJ, Saeed S, McCoy S, Osewa AA, Persaud A, Ahmed L. The effect of bariatric surgery on renal function. *Surgery for Obesity and Related Diseases* 2014; 10(5):808-813.

(32) Jackson S, le Roux C, Docherty N. Bariatric Surgery and Microvascular Complications of Type 2 Diabetes Mellitus. *Curr Atheroscler Rep* 2014; 16(11):1-9.

(33) Iaconelli A, Panunzi S, De Gaetano A et al. Effects of Bilio-Pancreatic Diversion on Diabetic Complications: A 10-year follow-up. *Diabetes Care* 2011; 34(3):561-567.

(34) Fenske WK, Dubb S, Bueter M et al. Effect of bariatric surgery-induced weight loss on renal and systemic inflammation and blood pressure: a 12-month prospective study. *Surgery for Obesity and Related Diseases* 2013; 9(4):559-568.

(35) Saliba J, Kasim NR, Tamboli RA et al. Roux-en-Y gastric bypass reverses renal glomerular but not tubular abnormalities in excessively obese diabetics. *Surgery* 2010; 147(2):282-287.

(36) Amin AM, Wharton HM, Clarke M, Syed A, Dodson PM, Tahrani AA. The impact of bariatric surgery on retinopathy in patients with type 2 diabetes: a retrospective cohort study. *Surgery for Obesity and Related Diseases*.

(37) Friedman AN, Moe S, Fadel WF et al. PREDICTING THE GLOMERULAR FILTRATION RATE IN BARIATRIC SURGERY PATIENTS. *Am J Nephrol* 2014; 39(1):8-15.

(38) Lieske JC, Collazo-Clavell ML, Sarr MG, Rule AD, Bergstralh EJ, Kumar R. Gastric Bypass surgery and measured and estimated GFR in women. *Am J Kidney Dis* 2014; 64(4):663-665.

(39) Coupaye M, Bouillot JL, Poitou C, Schutz Y, Basdevant A, Oppert JM. Is Lean Body Mass Decreased after Obesity Treatment by Adjustable Gastric Banding? *OBES SURG* 2007; 17(4):427-433.

(40) Guida B, Belfiore A, Angrisani L et al. Laparoscopic gastric banding and body composition in morbid obesity. *Nutrition, Metabolism and Cardiovascular Diseases* 15(3):198-203.

(41) Chaston TB, Dixon JB, O'Brien PE. Changes in fat-free mass during significant weight loss: a systematic review. *Int J Obes* 2006; 31(5):743-750.

(42) Vaurs C, Diméglio C, Charras L, Anduze Y, Chalret du Rieu M, Ritz P. Determinants of changes in muscle mass after bariatric surgery. *Diabetes & Metabolism* 2015.

Table 1: The impact of bariatric surgery on renal function in patients with T2DM. Change in eGFR was calculated as study-end – baseline values. Data presented as median (IQR) and mean±SD. P values were calculated using the related samples Wilcoxon Signed Rank test as the follow-up eGFR data was not normally distributed.

		Baseline	Follow-up	P value
eGFR (~~mls~~ml/min/1.73m^2)	Total population	86.0 (73.0-100.0) 86.5 ± 20.8	92.0 (77.0-101.0) 88.8 ± 18.9	0.003
	In eGFR ≤~~<~~ 60	48.0 (42.0-57.0) 47.7 ± 9.1	61.0 (55.0-63.0) 60.7 ± 14.0	0.004

Table 2: The impact of bariatric surgery on eGFR based on surgical procedure and baseline eGFR category. Data presented as mean ± SD. NA: Not applicable; LAGB: laparoscopic adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; LSG: laparoscopic sleeve gastrectomy. This analysis excluded the 8 patients that had the type of surgery missing from the database. P values were calculated using the related samples Wilcoxon Signed Rank test

Baseline eGFR ml/min/1.73m^2	Surgical procedure	Baseline eGFR ml/min/1.73m^2	Study-end eGFR ml/min/1.73m^2	P value
≤ 60	LAGB (n=11)	48.4 ± 9.4	56.4 ± 9.7	0.036
	LSG (n=0)	NA	NA	NA
	RYGB (n=4)	46.5 ± 9.5	72.5 ± 18.7	0.068
>60 to < 90	LAGB (n=44)	76.7 ± 8.1	84.1 ± 13.7	< 0.001
	LSG (n=5)	75.2 ± 8.8	79.6 ± 19.7	0.69
	RYGB (n=25)	78.0 ± 6.9	85.4 ± 14.5	0.003
90 to < 120	LAGB (n=36)	102.7 ± 7.3	95.8 ± 13.8	0.019
	LSG (n=4)	103.8 ± 9.1	100.3 ± 15.0	0.47
	RYGB (n=17)	99.5 ± 9.7	100.8 ± 14.1	0.19
≥ 120 (hyperfiltration)	LAGB (n=8)	128.3 ± 7.8	111.4 ± 19.3	0.036
	LSG (n=0)	NA	NA	NA
	RYGB (n=1)	128.0	150.0	NA

Table ~~3~~2: Summary of patients' baseline characteristics in the bariatric surgery group vs. routine care group. Data presented as mean±SD.*P value calculated using Mann Whitney U test as the data was not normally distributed

	Bariatric surgery (n=163)	Routine care (n=225)	P value
Age (years)	48.5±8.8	57.1±12.1	< 0.001
Women	66.9% (n=109)	42.7% (n=96)	< 0.001
HbA1c (mmol/mol)	59.6±19.6	66.1±16.0	< 0.001
BMI (Kg/m^2)	50.8±9.1	33.7±8.3	< 0.001
Follow-up (years)	3.0±2.3	2.5±0.7	0.02*

Table 43: Comparison of the eGFR and eGFR change between patients who had bariatric surgery vs. routine care in the total study population and in those with baseline eGFR ≤ 60 ml/min/1.73m^2. Data presented as mean±SD *P value calculated using Mann Whitney U test as the data was skewed ~~Table 4: Comparison of the eGFR and eGFR change between patients who~~

~~have baseline eGFR ≤ 60 mls/min/1.73m^2 and had bariatric surgery vs. routine care. *P value calculated using Mann Whitney U test as the data was skewed~~

Total study population	Bariatric surgery (n=163)	Routine care (n=225)	P value
Baseline eGFR ml/min/1.73m^2	86.5±20.8	86.1±26.5	0.89
Study-end eGFR ml/min/1.73m^2	88.8±18.9	81.0±27.5	0.001
eGFR change (study end minus baseline values) ml/min/1.73m^2	2.3±15.3	-5.1±11.0	<0.001*
Patients with baseline eGFR ≤ 60 ml/min/1.73m^2	Bariatric surgery (n=15)	Routine care (n=41)	P value
Baseline eGFR ml/min/1.73m^2	47.9±9.1	46.9±11.2	0.72
Study-end eGFR ml/min/1.73m^2	60.7±14.0	41.5±14.3	< 0.001
eGFR change (study end minus baseline values) ml/min/1.73m^2	12.8±13.2	-5.2±10.3	< 0.001*

Table 5: Summary of multiple linear regression assessing the impact of bariatric surgery on study-end eGFR. Outcome measure: study-end eGFR. R^2 for the model= 0.76

Variable	B	P
Baseline eGFR	0.822	< 0.001

Baseline BMI	-0.067	0.36
Baseline HbA1c	-0.385	0.33
Gender	0.603	0.65
Baseline age	-0.211	0.002
Follow-up duration	-1.813	< 0.001
Bariatric surgery vs. routine care	7.787	< 0.001

465