Bariatric and metabolic surgery and microvascular complications of type 2 *diabetes mellitus*

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Abstract

Introduction: Metabolic dysregulation is the defining characteristic of type 2 *diabetes mellitus* (T2DM) and may lead to microvascular complications, specifically retinopathy, nephropathy and neuropathy. Medical treatment and lifestyle interventions targeting risk factors for microvascular complications can yield therapeutic gains, particularly retinopathy and nephropathy. Bariatric/metabolic surgery is superior to the best medical treatment in several randomized controlled trials. Consequently, evidence of the effect of bariatric/metabolic surgery on microvascular complications is now emerging in the literature. **Methods:** A search of the recent published evidence base on the effects of bariatric/metabolic surgery on microvascular complications reveals further evidence that supports the efficacy of surgery in preventing the incidence and progression of albuminuria and preserving renal functional decline. **Discussion:** Data on retinopathy are ambivalent representing the potential in some cases for an influence of reactive hypoglycaemia over the retina but the majority of data emphasize that the metabolic control can halt the progression of the eye disease. A significant gap in the literature remains in relation to the effects of surgery on diabetic neuropathy, although some information sheds a light on the benefits secondary to the surgical metabolic control. **Conclusion:** Overall, although data so far is exciting, there is a pressing need for prospective randomized controlled trials examining long-term microvascular outcomes following bariatric/metabolic surgery in patients with T2DM.

Keywords: bariatric surgery; diabetic nephropathies; diabetic neuropathies.

Type-2 *diabetes mellitus*: complications and costs

The increase in the prevalence of fasting hyperglycemia observed since 1980 has been correlated with development and progress and associated with increases in the population's body mass index, suggesting that obesity is one of the drivers of type-2 *diabetes mellitus* (DM). Type-2 DM accounts for 85% to 90% of the cases of diabetes.[1] The diabetes/obesity epidemics and its ensuing complications have become a relevant public health issue. The CDC's National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP) recently reported that 29.1 million people in the United States have diabetes, and that 27.8% of the cases of the disease remain undiagnosed. Retinopathy, one of the comorbidities associated with type-2 DM, caused amaurosis in 4.2 million diabetic individuals aged less than 70 years. Almost 50,000 kidney transplants are carried out each year as a result of renal microvascular injuries in type-2 DM. Peripheral nerve damage may produce limb ulcerations and amputations. Sixty percent of the limb amputations performed in the United States are related to type-2 DM.[2,3]

The cost of diabetes in the United States in 2012 was estimated at USD 245 billion.[4]

Type-2 *diabetes mellitus* microvascular complications

The microvascular complications of type-2 DM affect mainly the retina (non-proliferative and proliferative retinopathy), the kidneys (diabetic nephropathy), and the nerves (central, peripheral, sensorimotor, and autonomic systems). Peripheral polyneuropathy is the most common manifestation. Complications arise as a function of the severity and time for which the patient has had the disease. Type-2 DM usually starts with progressive peripheral resistance to insulin, and moves on to postprandial hyperglycemia and hypertriglyceridemia with glucose toxicity and exhaustion of pancreatic beta cells. The endothelium is an important target of the noxious effects of excessively high levels of circulating glucose and lipids, and the site of origin of relevant microvascular complications.[5]

Diabetic nephropathy

Diabetic nephropathy can be defined as a persistent increase in albuminuria to levels above 30 mg of albumin per gram of urine creatinine. The glomerular filtration rate (GFR) decreases as a result of renal interstitial fibrosis, thus producing macroalbuminuria and possibly setting the stage for the onset of end-stage renal disease (ESRD). Macroalbuminuria is preceded by a long period (10-20 years) of progressive microalbuminuria (30-299 mg/g of urine creatinine). A prospective study carried out in the United Kingdom (UKPDS) revealed that 24.9% of the patients have microalbuminuria for 10 years, 5% develop macroalbuminuria, and less than one percent progress to ESRD.[6,7]

Diabetic retinopathy

Non-proliferative retinopathy, the most common complication for patients with type-2 DM, is characterized by microaneurysms in the retina and altered vascular permeability. Macular edema may occur and produce significant visual impairment.[8]

According to the UKPDS, 37% of the patients with type-2 DM have some degree of retinopathy at the time of diagnosis.[9]

Diabetic neuropathy

Diabetic neuropathy encompasses central nervous system disorders usually associated with injuries to the somatosensory system. In 50% of the cases the manifestations revolve around sensorimotor alterations showing a stocking-and-glove distribution. These manifestations occur due to microvascular degeneration and nerve fiber conduction deterioration, which decrease tactile stimuli and increase thermal thresholds, chronic pain, and paresthesia.[8,10]

Drug therapy and type-2 DM complications

The Diabetes Control and Complications Trial (DCCT)[11] showed that interventions focused on glucose management help control and prevent macro and microvascular complications. Four large clinical trials are frequently cited. The UKPDS[12] followed 3,867 patients submitted to strict glucose level management for over 11 years, with a target fasting glucose level < 110 mg/dl. The authors reported a reduction of 25% in the number of patients with microvascular complications, most of which associated with retinopathy. The Action in Diabetes and Vascular Disease (ADVANCE)[11] trial randomized 11,140 patients diagnosed with type-2 DM for a mean of eight years and followed them for five years with strict fasting glucose monitoring and a target glycated hemoglobin level (HbA1c) of 6.5%. No significant differences were found in the incidence of retinopathy, but cases of nephropathy were cut down by 21%. The Action to Control Cardiovascular Risk in Diabetes (ACCORD)[13] trial enrolled 10,251 patients diagnosed with diabetes for a mean of ten years. Thirty-five percent of the included patients had cardiovascular disease and 17% had microvascular involvement. The proposed therapy aimed to control glucose levels, with a target HbA1c level of 6%. The trial was suspended after three and a half years due to increased mortality in the group treated more intensively.

Steno-2[14] was the first large trial to randomize 80 patients with type-2 DM and microalbuminuria and offer intensified multimodal drug therapy (glucose control, angiotensin-converting-enzyme inhibitors, aspirin), dieting, and lifestyle changes, with set targets for HbA1c < 6.5%, blood pressure (BP) under 130/80 mmHg, total cholesterol level of 175 g/dl, and triglycerides at 150 mg/dl.[14] The patients were followed for eight years and had improved metabolic control, fewer cardiovascular events and microvascular complications, and 62% and 58% less cases of nephropathy and retinopathy, respectively.

Bariatric/metabolic surgery and resolution of risk factors for microvascular complications of type-2 *diabetes mellitus*

Bariatric surgery is currently the most effective procedure available to treat morbidly obese individuals. Randomized clinical trials showed the superiority of the Roux-en-Y gastric bypass (RYGB) procedure over drug therapy in the management of type-2 DM.[15-17] Prospective study Swedish Obese Subjects (SOS) showed how bariatric surgery decreased the progression of prediabetes to clinically established disease. Dyslipidemia and hypertension are the main risk factors for microvascular disease in type-2 DM associated with obesity. Schauer *et al*.[18] recently analyzed 120 patients diagnosed with type-2 DM for more than six months and HbA1c > 8% in a randomized controlled trial. The patients included in the study were given advice on lifestyle changes and were offered medical interventions. Sixty underwent RYGB surgery together with lifestyle changes and another group of 60 patients were offered drug therapy and lifestyle changes. Twelve months later, 28% of the individuals offered surgery and 19% of the subjects given drug therapy met the targets for HbA1c = 6%, LDL < 100 mg/dl, and systolic BP < 130 mmHg. The patients in the surgery arm met the targets using less medication. The better outcome of the group offered surgery was sustained three years into follow-up.[19]

Several other publications have described direct anti-diabetes measures independent from weight loss or the body mass index of the treated individuals.[20-24] The good outcomes of metabolic surgery, with fewer long-term macro and microvascular complications and reduced long-term mortality, has forced regulatory agencies to review the criteria in effect for the prescription of surgery based on the individual's weight. The severity of the associated diseases should be used as a reference in the prescription of any mode of treatment, be it drug therapy or surgery.[25]

Metabolic surgery is a new discipline that encompasses gastrointestinal procedures with direct effect on diabetes, initially independent from weight loss.

Regulated surgical procedures offered to morbidly obese individuals

Since the introduction of bariatric surgery, clinical practice and the medical literature have described promising and sometimes impressive outcomes in terms of the improvement and even remission of type-2 DM after surgery.[26,27]

A) Adjustable gastric banding (AGB) (figure 1).

Surgical technique

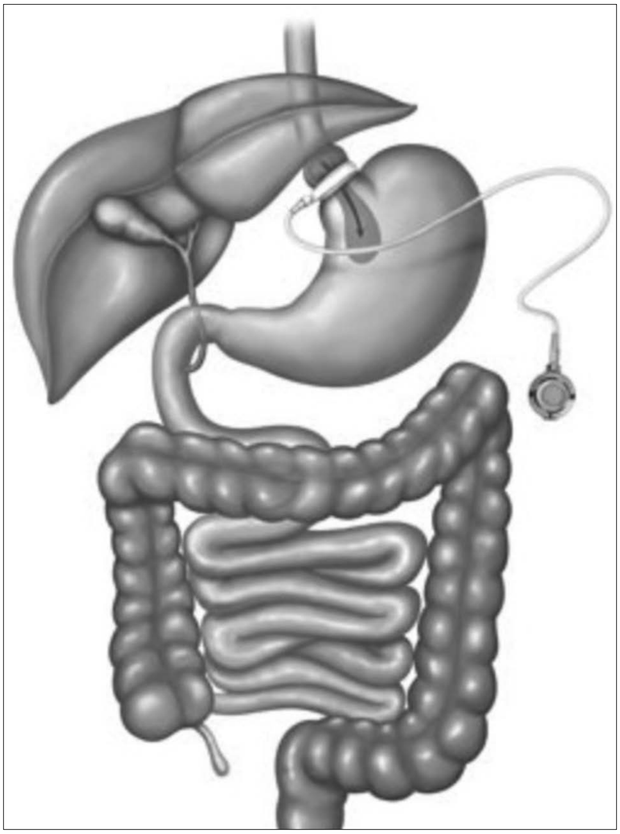
Once a pneumoperitoneum with approximately 15 mmHg of carbonic gas is created and appropriate visualization is established, the procedure is started with an incision in the peritoneum of the left diaphragmatic pillar. At this point, a retrogastric tunnel is created to allow the passage of the band catheter. The stomach is isolated by the catheter, but the fat of the lesser omentum is kept together. The second stage of band placement is then initiated. A 30-ml balloon is inflated inside the stomach and pulled to the gastroesophageal junction de volume to shape the new stomach. Below the balloon, in the right margin of the stomach, the fat of the lesser omentum is isolated and the band catheter is pulled so that the stomach is isolated without excessive fat in its circumference. Then two stiches with non-absorbable 2-0 suture wire are applied to unite the ends of the stomach over the closed band, while another stich attaches the fundus of the stomach to the left pillar.

Results

Several retrospective and observational studies have reported type-2 DM remission rates of 50% in patients followed from 12 to 36 months. However, the definitions given to controlled type-2 DM varied significantly, with parameters ranging from glucose (HbA1c < 7) to metabolic (HbA1c, LDL, and multifactorial BP) control.

In 2008, a randomized controlled trial by Dixon *et al*.[15] compared 60 patients with BMIs in the 30-40 kg/m^2 range. The patients were divided into two groups, one given behavioral modification and drug therapy

Figure 1. Adjustable gastric banding.



and the other AGB. After 24 months of follow-up, 73% of the individuals in the AGB group achieved remission, defined as fasting glucose < 126 mg/dL and HbA1c < 6,2% without anti-diabetic medication, against only 13% of the patients in the conservative therapy group. As expected, after purely restrictive procedures, remission was directly associated with greater weight losses. The patients included in this study had a short history of type-2 DM and had been treated only with oral anti-diabetic medication.

B) Roux-en-y gastric bypass (RYGB) (figure 2)

Surgical technique

This procedure may be performed in a minimally invasive fashion. It involves the creation of a gastric pouch of 20-50 ml in volume and a bypass in the distal stomach and proximal bowel with varying loop sizes. Then a usually precolic enteroanastomosis and a gastrojejunal anastomosis are constructed, either manually or with the aid of a linear or circular stapler.

Results

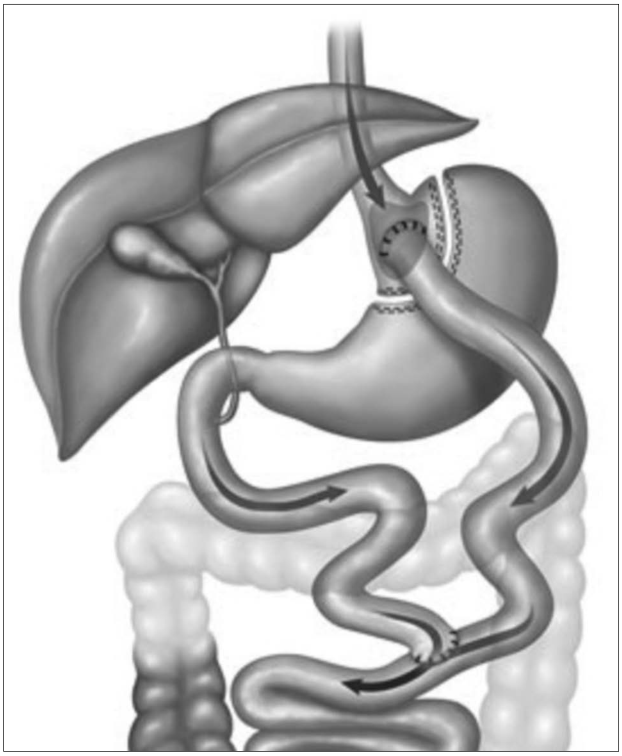
RYGB is the most commonly performed bariatric procedure in Brazil and the world. It is also the procedure with the longest follow-up and the most consistent and reproducible results.

In 1995, Pories *et al.*[26] studied 608 morbidly obese individuals offered RYGB followed for 14 years. The outcomes of the procedure were described not only in terms of lasting weight loss, but also in improved glucose level control in diabetic patients (82.9%) and in individuals with glucose intolerance (98.7%), and improvement or resolution of other comorbidities such as high blood pressure, sleep apnea, heart failure, arthritis, and infertility. Similarly, in 2003 Schauer *et al.*[28] described a type-2 DM remission rate of 83% after five years, particularly seen in patients more recently diagnosed with the disease and individuals off insulin. In a study by Higa *et al.*,[29] 83% of the individuals improved or achieved remission after RYGB. Approximately 67% of the patients had their glucose levels controlled ten years into follow-up. Several other authors reported high rates of resolution or improvement from type-2 DM after RYGB.[30-36]

The Swedish Obese Subjects (SOS) trial,[37] one of the most respected studies on bariatric surgery, enrolled 4,047 prospective patients followed for over a decade. Patients in the surgery group experienced significantly greater and longer-lasting weight loss (25% weight loss ten years after undergoing RYGB) than the individuals in the control group (1.6% weight gain). They also did better in parameters such as glucose and insulin levels, hypertriglyceridemia, waist circumference, hypertension, and LDL reduction - some of the criteria used in the diagnosis of metabolic syndrome - and had decreased incidences of obesity after metabolic surgery. Additionally, after two years of follow-up none of the patients in the surgery group had diabetes, *versus* five percent of the individuals in the control group. This preventive effect was sustained ten years into follow-up, with the surgery group having one third of the chance of having diabetes of the group given conservative therapy.

In 2004, Buchwald *et al.* published a meta-analysis[27] in which 22,094 patients submitted to bariatric surgery were analyzed. The results published in the SOS study were confirmed, as 76.8% of the patients achieved remission from diabetes, 86.0% achieved remission or improved, 70% improved from dyslipidemia, 61.7%

Figure 2. Roux-en-Y gastric bypass.



ceased to suffer from high blood pressure, 78.5% no longer had hypertension or improved their BP levels, and 85.7% were no longer diagnosed with obstructive sleep apnea syndrome. Other authors also described improvements in dyslipidemia and lower LDL levels in approximately 28% of the cases.[38]

Another recent report from the SOS study showed that bariatric procedures and RYGB in particular can effectively prevent type-2 DM.[39] In a longitudinal prospective study, the incidence of type-2 DM in disease-free obese individuals after surgery was 6.8 cases for every 1,000 individuals, *versus* 28.4 cases for every 1,000 subjects in the control group. Interestingly, the BMI had a smaller impact on the reduction of risk of type-2 DM. The patients with elevated fasting glucose and insulin levels were at lower risk of developing type-2 DM than the individuals with higher BMIs.

C) Vertical gastrectomy (VG) (figure 3)

Surgical technique

This procedure may be performed using a minimally invasive technique. It consists of a longitudinal resection of the greater curvature of the stomach, starting three or four centimeters above the pylorus going all the way to the gastroesophageal junction.

Results

VG, also known as the duodenal switch procedure, was originally described as the first stage of an RYGB procedure for super-obese individuals or clinically severe patients, but a great deal of these subjects improved markedly from their comorbidities and lost quite a bit of weight after it, thus rendering the second stage of the procedure or additional surgery unnecessary.[40]

Some systematic reviews and meta-analyses reported short-term remission rates from type-2 DM of 70% to 80% after VG.[41,42] VG is a procedure seemingly easier than other metabolic procedures, but it requires good knowledge of the anatomy and technical refinement from the surgeons carrying out the procedure. It is by no means a simpler procedure. There is reasonable controversy about its mode of action. Several authors have described metabolic control neuroendocrine mechanisms,[43,44] while others believe the improvement from type-2 DM derives exclusively from weight loss.[45]

In 2012, Leonetti *et al.*[46] compared the levels of metabolic control produced from VG and conservative treatment, with 80% remission from type-2 DM (HbA1c < 7, without medication) reported for patients offered surgery *versus* 1.7% for the group administered drug therapy.

Lee *et al.*[47] reported more modest results after following patients submitted to VG for 12 months, with a rate of type-2 DM remission of 50%. The same authors compared RYGB and VG in a group of diabetic obese patients and showed that for equal levels of weight loss RYGB was statistically superior to VG in terms of controlling type-2 DM, implying that weight loss might not be the only factor in gastric bypass procedures (RYGB).

D) Biliopancreatic diversion with or without duodenal switch (figures 4 and 5)

Both procedures reduce the absorption of calories and nutrients and restrict food intake. The biliopancreatic diversion procedure described by Scopinaro consists of resecting part of the stomach and creating a common 50-cm long absorption channel. The duodenal switch procedure is a broader vertical gastrectomy designed to create a common 100-cm long absorption channel to attenuate the intensity of malabsorption when compared to the Scopinaro procedure.

Figure 3. Vertical gastrectomy.

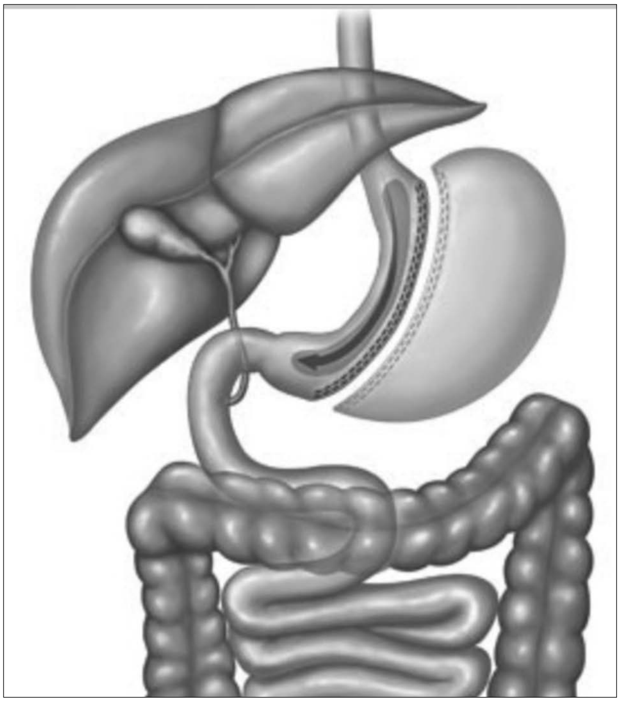
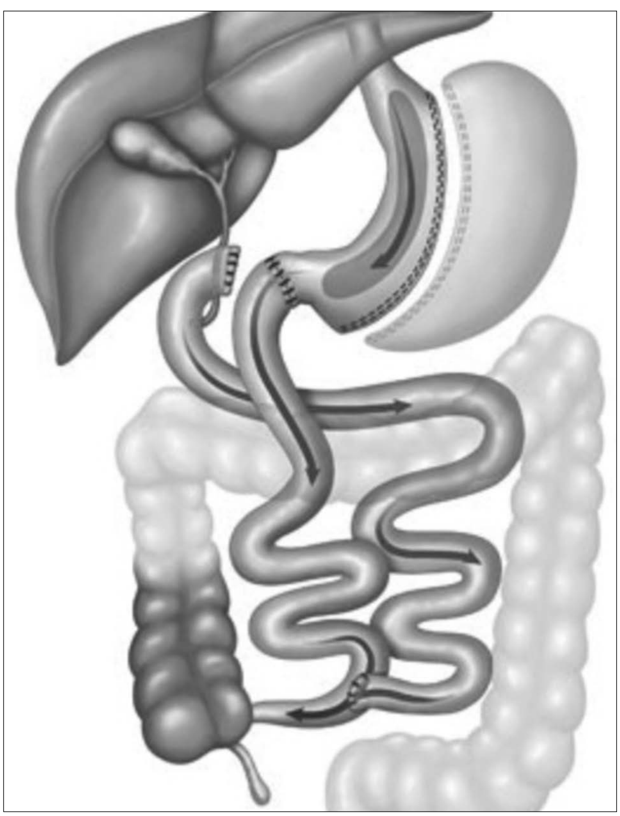


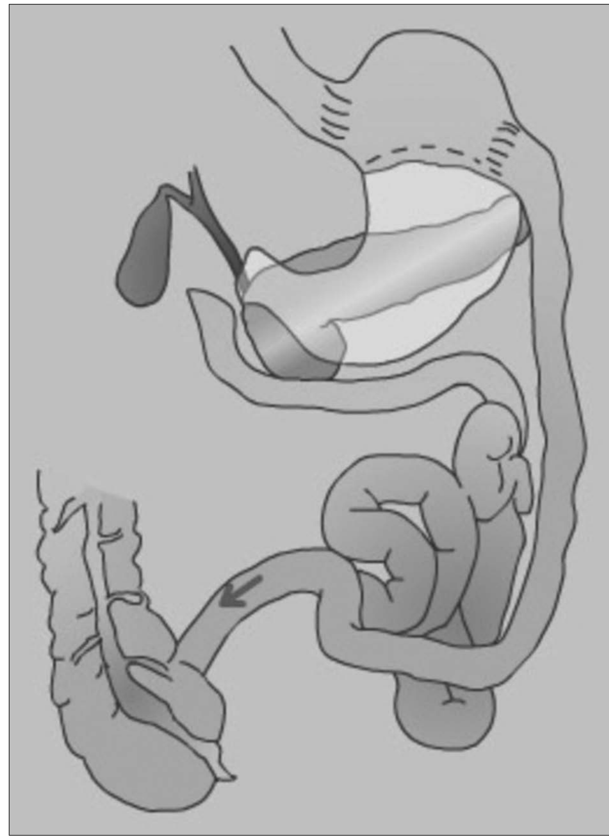
Figure 4. Biliopancreatic diversion with duodenal switch.



Results

The reported type-2 DM resolution rates observed after the Scopinaro biliopancreatic diversion or the duodenal switch procedure range between 85% and 96%.[48,49] Despite the metabolic control qualities of these procedures, the described medium and long-term severe nutritional complications of biliopancreatic diversion procedures have limited their use in favor of other procedures such as RYGB, which also offers good results and a superior postoperative risk profile.[50]

Figure 5. Scopinaro biliopancreatic diversion.



Systematic review of recent data on the impact of bariatric surgery on microvascular complications arising from type-2 *diabetes mellitus*: objectives and approach

The section below presents a summary of the clinical data published since 2011 on the effect of bariatric surgery over microvascular complications arising from type-2 DM. The data described herein were collected from a systematic search performed on PubMed using the following keywords: Roux-en-Y gastric bypass, vertical gastrectomy, biliopancreatic diversion (BPD) with or without duodenal switch, bariatric surgery, metabolic surgery, diabetes microvascular complications, retinopathy, nephropathy, neuropathy. Classifiers: clinical trial, observational study, comparative study, randomized controlled trial, phase-I clinical trial, phase-II clinical trial, phase-III clinical trial. The results of the 16 studies matching the search criteria are summarized below.

Prospective studies (Table 1)

The most compelling prospective study published to date on the effects of bariatric surgery *versus* conventional conservative therapy on microvascular complications is a non-randomized case-control study by Iaconelli *et al.*,[51] which looked into the effects of BPD on urinary albumin excretion and the glomerular filtration rate of 50 obese patients recently diagnosed with type-2 DM. Increased serum creatinine levels associated with signs of macrovascular disease were observed in 39.3% of the individuals in the conservative therapy group *versus* 9% of the subjects in the surgery group, while the delta GFR was -45.7 ± 18.8 in the conservative therapy group *versus* 13.6 ± 24.5% in the second group, reflecting the preservation of the GFR among patients offered surgery. Although 14.3% of the patients in the control group (*versus* 31.8% of the patients in the BPD group) had microalbuminuria at the start of the study, after two years of follow-up the situation had reversed in the conservative care group, with the incidence of microalbuminuria soaring to 28.6%, while in the bariatric/metabolic surgery group the incidence dropped to 9.1%. None of the individuals in the BPD group had microalbuminuria after ten years of follow-up, while in the control group the situation had uniformly worsened.

Amor *et al.*[52] carried out a prospective observational study with 96 patients with type-2 DM offered RYGB or VG. The study aimed to describe the impact of the procedures and of weight loss on urinary albumin excretion. The baseline albumin/creatinine ratio (ACR) was 85.7 ± 171 mg/g with an ACR > 30 mg/g (microalbuminuria) observed in 45.7% of the enrolled subjects. Twelve months later the ACR was significantly lower (42.2 ± 142.8 mg/g) and the number of patients with an ACR > 30 mg/g dropped by 41.5%.

A prospective cohort study by Fenske *et al.*[53] assessed the changes occurred in 12 months in the bodyweight, blood pressure, serum and urinary cytokine levels of 30 morbidly obese individuals offered adjustable gastric banding (AGB) (n = 13), RYGB (n = 10), or VG (n = 11) procedures. In regards to indicators of renal microvascular disease, the significant reductions seen in bodyweight and blood pressure throughout the 12 months of the study were accompanied by decreases in the levels of C-reactive protein and the urinary and serum levels of macrophage migration inhibitory factor, monocyte chemotactic protein-1, and chemokine ligand 18. Nine patients had baseline serum cystatin C levels > 0.8 mg/l, an indicator of renal function involvement, but significant improvements were seen after 12 months of follow-up.

Retrospective studies (Table 2)

Johnson *et al.*[54] carried out a large study with obese patients diagnosed with type-2 DM. The microvascular outcomes of 2,580 subjects submitted to bariatric procedures and 13,371 non-operated controls meeting identical enrollment criteria seen between 1996 and 2009 were compared. The microvascular outcomes were defined in terms of new diagnosis of amaurosis in at least one eye, retinal procedures, amputation unrelated to trauma, or placement of a permanent dialysis access. Surgery was associated with significant decrease in microvascular events (adjusted HR of 0.22; 95% CI 0.09-0.49).

Miras *et al.*[55] analyzed 84 patients with type-2 DM submitted to bariatric surgery for a period of 12 to 18 months. Fifty-nine of the included patients had undergone RYGB (70.2%), 19 VG (22.6%), and 6 AGB (7.1%) procedures. Pre and postoperative (12-18 months) two-field retinograms and ACRs were analyzed. Five (7.5%) of the 67 patients with complete retina data improved from their retinal involvement, one (1.5%) worsened, and 61 (91.0%) remained unchanged. Twenty-eight individuals had retinopathy before surgery. Five (17.8%) improved, one (3.6%) worsened, and 22 (78.6%) remained unchanged. The mean retinopathy score for the entire group decreased significantly from 4.7 ± 0.6 to 3.3 ± 0.5. A subgroup of patients submitted to RYGB with albuminuria before surgery had a significant 3.5-fold ACR decrease after surgery.

Varadhan *et al.*[56] looked into the impact of bariatric surgery (RYGB and VG) on the diabetic retinopathy

Table 1 Prospective studies. Bariatric/metabolic surgery, and microvascular endpoints

Author	Number of patients and length of follow-up	Procedures	Microvascular endpoints
Iaconelli *et al.*[51]	50; 2 years	BPD* *vs.* Control	Lower microalbuminuria in surgery group
Amor *et al.*[52]	96; 2 years	RYGB**/VG***	Lower ACR#
Fenske *et al.*[53]	30; 1 year	AGB ¶/RYGB**	Improved inflammatory markers

* Biliopancreatic diversion; ** Roux-en-Y gastric bypass; *** Vertical gastrectomy; # Albumin/creatinine ratio; ¶ Adjustable gastric banding.

Table 2 Retrospective studies. Bariatric/metabolic surgery, and microvascular endpoints

Author	Number of patients and length of follow-up	Procedures	Microvascular endpoints
Johnson *et al.*[54]	2,580; 15 years	Several; not described	Decreased retinopathy and kidney disease
Miras *et al.*[55]	84; 2 years	RYGB/VG/AGB	Decreased ACR# and stable retinopathy
Varadhan *et al.*[56]	23; 3 years	Several; not described	Variable outcomes of regression, stabilization, and worsening of retinopathy
Brethauer *et al.*[57]	215; 5 years	RYGB**/VG***/AGB¶	Decreased ACR#; Stabilization of retinopathy and regression or stabilization of nephropathy
Heneghan *et al.*[58]	52; 66 months	Several, predominantly RYGB***	Significant regression of nephropathy
Carlsson *et al.*[59]	1,498 surgery *vs.* 1610 controls; 15 years	Several	Decreased microalbuminuria in surgery group
Stephenson *et al.*[60]	23; 3 years	AGB¶	Decreased microalbuminuria
Jose *et al.*[61]	25; 4 years	BPD*	Improved renal function
Thomas *et al.*[62]	40; 1 year	Not described	Stabilization or regression of retinopathy

* Biliopancreatic diversion; ** Roux-en-Y gastric bypass; *** Vertical gastrectomy; # Albumin/creatinine ratio; ¶ Adjustable gastric banding.

statuses of 23 patients followed for over three years. Two patients (9%) had new cases of retinopathy and in two (9%) the pre-existing disease worsened. Thirteen (59%) patients were not diagnosed with retinopathy before of after the procedure and in three (14%) individuals the retinal involvement remained stable. Two patients (9%) improved from their retinal involvement after surgery.

Brethauer *et al.*[57] reported the five-year outcomes of patients with type-2 DM submitted to bariatric surgery (RYGB n = 162; AGB n = 32; VG n = 23) between 2004 and 2007, showing improvement from diabetic nephropathy in 53% of the patients and stabilization of the disease in the remaining 47%.

Heneghan *et al.*[58] followed 52 obese patients with type-2 DM for five years after bariatric surgery with seriated ACR tests. Nephropathy was diagnosed in 37.6% of the patients before surgery, and 58.3% had the involvement resolved after a mean of 66 months. The incidence of microalbuminuria was 25%.

In a substudy after the SOS trial, Carlsson *et al.*[59] looked into the 15-year incidence rates of albuminuria of 1,498 patients offered bariatric surgery and 1,610 controls without albuminuria provided conservative care. The procedures included AGB (18%), vertical sleeve gastrectomy (69%), and RYGB (13%). The enrolled individuals were followed for a mean of 10 years, with follow-up rates of 87%, 74%, and 52%

at two, ten, and 15 years, respectively. Albuminuria was observed in 246 subjects in the control group and in 126 patients in the bariatric surgery group (hazard ratio, 0.37; 95% confidence interval, 0.30-0.47).

Stephenson *et al.*[60] followed 23 obese patients diagnosed with type-2 DM and established renal disease for three years to analyze the effects of AGB on albuminuria. Two of the seven patients with macroalbuminuria at baseline moved to normal urine albumin levels, two to microalbuminuria, and three remained with macroalbuminuria after 36 months of follow-up. Nine of the 16 patients with microalbuminuria at baseline moved to normal urine albumin levels, six remained with microalbuminuria, and one progressed to macroalbuminuria.

Jose *et al.*[61] assessed the renal function of 25 patients submitted to BPD followed for a mean of four years. Serum creatinine decreased by 16.2 ± 19.6 nmol/l and the estimated GFR improved by 10.6 ± 15.5 ml/min/m^2.

Hou *et al.*[62] looked into the GFR of 233 bariatric surgery patients followed for over 12 months. Patients were stratified at baseline considering their eGFR and chronic kidney disease (CKD) statuses. Sixty-one patients were categorized as having hyperfiltration (GFR 146.4 ± 17.1 ml/min/1.73 m^2), 127 were placed in the normal GFR range (105.7 ± 9.6 ml/min/1.73 m^2), 39 had stage-2 CKD (76.8 ± 16.7 mL/min/1.73 m^2), and six had stage-3 CKD (49.5 ± 6.6 ml/min/1.73 m^2). After bariatric surgery, the GFR in the hyperfiltration group decreased to 133.9 ± 25.7 mL/min/1.73 m^2; in the normal GFR group, it increased to 114.2 ± 22.2 mL/min/1.73 m^2; in the stage-2 CKD group, the GFR increased to 93.3 ± 20.4 mL/min/1.73 m^2; and in the stage-3 CKD group, it increased to 66.8 ± 19.3 mL/min/1.73 m^2.

Thomas *et al.* carried out a pilot retrospective study to analyze the incidence and progression of diabetic retinopathy 12 months after bariatric surgery in patients offered the procedure between 1998 and 2012. A group of 40 individuals with retina test results before and after surgery was identified. Only four of the individuals without retinopathy before surgery (n = 26) had minimal disease progression after surgery. Retinopathy did not progress in the subjects with minimal disease before surgery (n = 9), and five individuals with established disease improved. The disease progressed in one individual with severe retinopathy and in two with pre-proliferative disease.

Conclusions

The data presented above speak in favor of a role for bariatric and metabolic surgery in reducing the rates of renal disease in patients with type-2 DM and early-stage renal disease. The most remarkable and reported finding is the potential role these procedures have in albuminuria remission. It is not clear, however, if weight loss alone supports decreases in proteinuria. A meta-analysis with 522 patients from 13 trials looked into different weight loss methods and reported a reduction of 1.1 mg in albumin excretion for every 1 kg of bodyweight lost; however, the impact of surgery on renal function and on evidence of renal inflammation suggests the effects of surgery on the kidney are multifactorial and not exclusively related to weight loss. The renoprotection offered by incretins such as GLP-1 described in preclinical animal models is promising.

Adverse postoperative events such as acute kidney injury and hyperoxaluria may negatively impact previously injured kidneys in the long term. However, there is not sufficient data on the advantages and disadvantages of bariatric and metabolic procedures for patients with reduced renal reserves.

Despite the positive nature of the data on the incidence of retinopathy after surgery, when established after surgery the disease may progress and become untreatable due to microvascular aggression not detected at the time of surgery. Retinopathy can be selectively more sensitive to episodes of reactive hypoglycemia than the kidneys after surgery or drug therapy, which, in some cases, may account for the progression of the disease. Additionally, there might be less room for injury resolution in the retina than in the kidneys due to differences in the epithelial regeneration ability of the retinal and renal nerve fibers.

Very little has been published on diabetic neuropathy after bariatric surgery. Most of the discussions in the literature revolve around the potential micronutrient deficiencies introduced by surgery possibly associated with the onset of neuropathies.

Although the evidence on the benefits of bariatric surgery is growing, randomized clinical trials should be organized to compare the relative benefits of drug therapy *versus* surgery and drug therapy combined, along with the microvascular complications experienced by obese patients diagnosed with type-2 DM.

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