ORIGINAL ARTICLE

Effects of Metabolic Surgery on Diabetic Nephropathy: Preliminary Experience at the General Hospital of San Juan Del Río

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ABSTRACT

Background: Diabetes mellitus type 2 (DMT2) is the main cause of nephropathy in the world and metabolic surgery is the best option for the treatment of DMT2, demonstrating beneficial effects in angiopathy, neuropathy, and diabetic nephropathy. The mechanisms of action include the secretion of enterohormones, bile acids, modification of the intestinal microbiota, and neurohumoral effects. Glucagon-1-like peptide acts at renal level favoring natriuresis, stabilizing podocytes by decreasing blood pressure and proteinuria. **Objective:** The objective of this study is to report the effects obtained from 30 cases of diabetic nephropathy, after the intervention of bipartition of intestinal transit, to modify the natural history of chronic kidney disease in the second level hospital, General Hospital of San Juan del Río. **Materials and Methods:**Inclusion criteria of patients with 26 DMT2 and diabetic nephropathy according to the Clinical Practice Guidelines 2014 were selected with decreased renal function 27 expressed by a glomerular filtration rate (GFR) <60 mL/min/1.73 m2, independently of the presence of markers of renal damage 28 (histological alterations, albuminuria-proteinuria, alterations of urinary sediment or alterations in imaging studies), or as the 29 presence of renal damage independently of GFR. **Results:** We report the first Mexican series of patients undergoing Intestinal Bipartition Transit (BTI) for coadjuvant management of DMT2, finding complete remission rates of 62%. BTI is the simplest and safest metabolic surgery for the management of DM, and it is possible to perform it with an adequate safety profile in a prototypical general hospital in Mexico. **Conclusions:** The accumulated evidence suggests that treatment of patients with diabetic nephropathy through Bipartition of Intestinal Transit is associated with the reduction of GFR, as well as preservation of renal function and decrease in cardiovascular events.

Key words: Diabetes mellitus type 2, diabetic nephropathy, enterohormones, metabolic surgery, renoprotection

INTRODUCTION

Diabetes mellitus type 2 (DMT2) is the main cause of nephropathy in the world.[1,2] According to the evidence available up to date, metabolic surgery is the best option for DMT2 treatment and diabetic nephropathy. Intestinal Bipartition Transit Surgery (BTI) is a simple and highly effective procedure for the control of DMT2 and consists in the anatomical modification of the small intestine making a latero-lateral anastomosis between the jejunum and ileum, improving the secretion of insulin on re-establishment of the kinetics of incretins, as is the glucagon-1-like peptide (GLP-1); it increases the concentration of bile acids, modifies the microbiota, and acts in the regulation of the appetite through GLP-2, oxyntomodulin, and peptide YY (PYY). Unlike gastric bypass and biliopancreatic diversion, BTI does not favor blind loops or malabsorption because it does not exclude intestinal segments.[3,4] The increase of GLP-1 can

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exert favorable renal effects that could contribute to reduce the risk of diabetic nephropathy.[5,6]

According to the International Diabetes Federation, China, India, United States, Brazil, Russia, and Mexico, are the countries with the highest number of DMT2. By severity, 1.4%, which is equivalent to 89,000 Mexicans, will enter dialysis due to a preventable cause.[7-9] Santoro postulated the principles of metabolic surgery defining adaptive procedures as those that do not depend on restriction, malabsorption, stenosis, or prosthesis use. Although some authors continue to equate the terms bariatric with metabolic, metabolic procedures have little impact on weight and can be used in patients with normal weight, overweight, or obesity.[10-13] The pure metabolic procedures alter the way the intestine works by modifying its anatomy (ileal interposition and BTI) without favoring malabsorption. Digestive adaptation is a surgical technique for obesity based on this logic. Therefore, they cannot be categorized for any of those already known as restrictive, mixed, or malabsorptive.[14-16]

Guilbert *et al*.[4] presented a series of Mexican cases that included 63 patients. Operating with 3 variants associated with each other, obesity, reduced high-density lipoprotein and high glucose , everyone with DMT2. Statistically significant improvement in metabolic syndrome and its components analyzed. The prevalence of this syndrome was 6.3% at 12 and 24 months.[17] It should be noted that more than half of the patients who are candidates for bariatric surgery have metabolic syndrome. Bariatric surgery improves the metabolic syndrome and its components with results that last more than 2 years. Other metabolic parameters important for cardiovascular risk during the 2 years are also improved.

There is a direct relationship between weight loss and improvement of metabolic syndrome.[18] The procedure, which our study proposes, dates from a major surgery that is indicated, especially, in patients with obesity Grade II with a body mass index (BMI) >35 points, with comorbidities such as diabetes and hypertension, or patients with BMI of 40 points or more, with excellent bibliographic results in the reduction of body weight significantly, up to 75%, after 5 years of intervention.[19-22]

The BIT surgery is based on the principle of endogenous stimulation of enterohormones that interact and stimulate the production and regeneration of pancreatic beta cells, and the renoprotective effect has been documented by decreasing the levels of reactive oxygen species. Recalling that, obesity by itself is a pro-inflammatory agent.[23-26]

The GLP-1 is secreted in response to ingestion of nutrients with intestinal specialization in the enteroendocrine system, called L-cells; Likewise lipids and sugars are the most potent stimulators of GLP-1. This hormone is produced from the post-translational process of preproglucagon. Once secreted, the active form of the hormone is practically degraded by dipeptidyl peptidase-4.[27-31]

The incretin effect of GLP-1 is due to the following mechanism, where insulin potentiates its response, to oral glucose intake, compared to insulin secretion in response to intravenous administration. This results in an increase in levels of glucose delivery to the large intestine. GLP-1 exerts glucoregulatory actions delaying gastric emptying, as well as anorexigenic effect.[32-35] Therefore proliferation and activation of PYY seems to play an important role, being an intestinal hormone, which function is suppression of the appetite, decreasing by this path, the consumption of food. Statistically significantly reducing up to 30% of food intake in the worldwide studies reported.[36,37]

Based on physiological data and supported by evolutionary data, this procedure creates a proportionally reduced gastrointestinal (GI) tract that amplifies post-prandial neuroendocrine responses. Leave the basic GI functions unharmed. It reduces the production of ghrelin and resistin, taking more nutrients to be absorbed distally, improving the secretion of GLP-1 and PYY.[38,39]

The procedure is simple, the complication rates are low, and in the world literature for procedures of this nature as in this case, there were no direct deaths for this event.[40] The increase of GLP-1 can exert favorable renal effects that could contribute to reduce the risk of diabetic nephropathy, so the surgical intervention could be an excellent tool.[41-44]

A further study supports this theory, the group of collaborators Ramírez *et al*. Which reported the intervention of 200 patients, providing remission of DMT2, 57.9, 61.1 and 60%. For weight loss, there were differences between the groups when using the BMI and the percentage of excess weight loss but not with the percentage of total weight loss. The non-metabolic and clinical data improved without differences. Concluding from this series, that the metabolic, lipid, and clinical profiles associated with obesity show a similar improvement, 1 year after the gastric laparoscopic bypass, despite the different initial BMI. The remission of diabetes and the percentage of total weight loss were also similar. Likewise, there is a homogeneous improvement in almost all parameters analyzed (metabolic, lipid, and clinical profiles) of patients undergoing gastric bypass after 12 months, despite presenting different degrees of obesity at the beginning of the study. Weight loss and remission of diabetes are also similar between groups. In a prominent way, it is mentioned that the initial BMI does not have a solid influence on the improvement in most of the data presented in this study, supporting, of course, our study protocol where although the sample is small, this point is highlighted.[45-47]

Study design

This was a report of 30 cases of the General Hospital San Juan del Río, Querétaro, from January 2016 to January 2017.

MATERIALS AND METHODS

Inclusion criteria

The inclusion criteria were selected patients with DMT2 and diabetic nephropathy according to the 2014 Mexican Clinical Practice Guide. We selected patients with decreased renal function expressed by glomerular filtration rate (GFR) <60 mL/min/1.73 m^2, regardless of the presence of damage markers. Kidney damage was documented by (histological alterations, albuminuria, proteinuria, alterations of urinary sediment, or alterations in imaging studies), or as the presence of kidney damage independently of GFR. These alterations are persistent for at least 3 months.As well, it was taken into account the clinical practice guide for the management of diabetes without morbid obesity, adding intestinal segmental exclusion as an approved technique for metabolic surgery. Including the precise indications for bariatric surgery of: Age between 18 and 55 years, BMI> 40 kg/m2 or between 35 and 45 kg/m2 associated with comorbidities (systemic arterial hypertension, joint disease, dyslipidemia, susceptible to improving weight loss. Register failure or therapeutic failure in weight loss or in the ability to maintain weight loss for a period >18 months, after an individualized and properly supervised pharmacological and non-pharmacological treatment, demonstrate strict medical control (clinical and laboratory) during a continuous period of >6 months in those subjects with metabolic and cardiopulmonary comorbidity demonstrate decision capacity and have adequate family support network. Understand and undergo a medical and psychological evaluation before and after surgery. Adhere to nutritional and psychological control and monitoring program. Fertile age must agree to avoid pregnancy for at least 1 year after surgery.[101-103]

The definitions of remission and improvement of DMT2 were based, as suggested by the criteria established by the American Diabetes Association in 2009 and clinical practice guidelines, where partial remission is defined as hyperglycemia below the threshold of DMT2 (100–125 mg/dL), an hemoglobin A1c (HbA1c) <6.5% without medication, for at least 1 year. Complete remission is a normal blood glucose level (<100 mg/dL) with HbA1c <5.7% and no medication, for at least 1 year. Improvement was defined as the decrease in the number and/or dose of medications (including insulin), associated with better control of glucose levels.[48-52]

Exclusion criteria

Patients with diabetic nephropathy of the General Hospital San Juan Del Río who did not accept the surgical intervention were excluded from the study.

Selection of the source, methods, techniques, and procedures for collecting information

Data collection

Data were compiled from clinical electronic records of patients submitted to Bipartition of Intestinal Transit in the General Hospital San Juan del Río in the year 2016–2017.

Surgical technique

The German group of Melissas *et a*l. 2012 reported the feasibility of a simple jejunoileal anastomosis from side to side in individuals not morbidly obese for DMT2, and it was studied in six diabetic patients with BMI 28–32 kg/m^2.[53-56]

The following is the surgical procedure used: Pure metabolic surgery (bipartition of intestinal transit).

It begins with the exploration of the abdominal cavity, and then the jejunum–ileum is measured from the fixed loop to the ileocecal valve. It is suggested to gently elongate and measure the antimesenteric border.[57-59]

Subsequently, the site of the anastomosis was decided 100 cm from the jejunum to the ileum at the level of the Treitz angle, standardizing the procedure in the 3 cases reported. This allows obtaining 1/3 of the jejunum with 2/3 of the ileum for the resulting length (this must be 30% and 40% of the initial length). Within the complications, if it becomes <30%, there will be dysbiosis, while if it is higher, it will not have any effect.[60-64]

Therefore, there is no DE functionalizing loop because it is bipartition. In Figures 1 and 2, it is suggested to use a stapler for GI anastomosis of 55 mm. The enterotomy and omentectomy are performed for the insertion of the stapler. Following this, the stapler is activated without initiating the cut and the mesenteric gap is then closed with polydioxanone suture (PDS) from 2–0 to 3–0 with non-anchored continuous suture, avoiding causing ischemia by transfection of mesenteric vessels. Before concluding, two seromuscular points are placed 7–10 cm from the ends of the anastomosis. We proceed to the first closure of the other end of the mesenteric gap. Finally, the stapler is activated and removed. The enterotomy closes in two planes with PGA 3–0 and PDS 3–0. The impermeability of the anastomosis is verified. The correct hemostasis is verified [Figure 1].

At the end of the procedure, monitoring and surveillance are available, and the second day of intervention is discharged. BTI does not favor blind loops, however, according to intestinal length in continuity, there may be deficiencies of micro- and macronutrients such as iron, zinc, Vitamins B and D, as well as calcium and albumin. A complication described in the approach is dysbiosis with the generation of diarrhea and flatulence.[65-67]

DISCUSSION AND JUSTIFICATION

According to Machytka et al. meta-analysis demonstrate the majority of patients with DMT2 are obese. Studies show that bariatric surgery is superior to medical treatment for the remission of DMT2.[68-70] A significant reduction in the level of glycosylated hemoglobin was observed in all

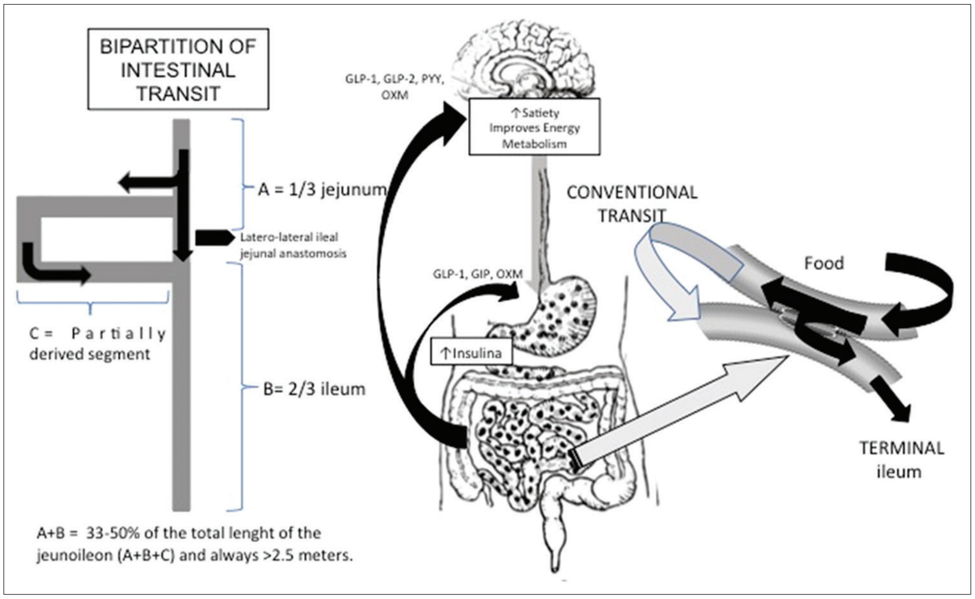


Figure 1: Conventional transit and intestinal transit bipartition

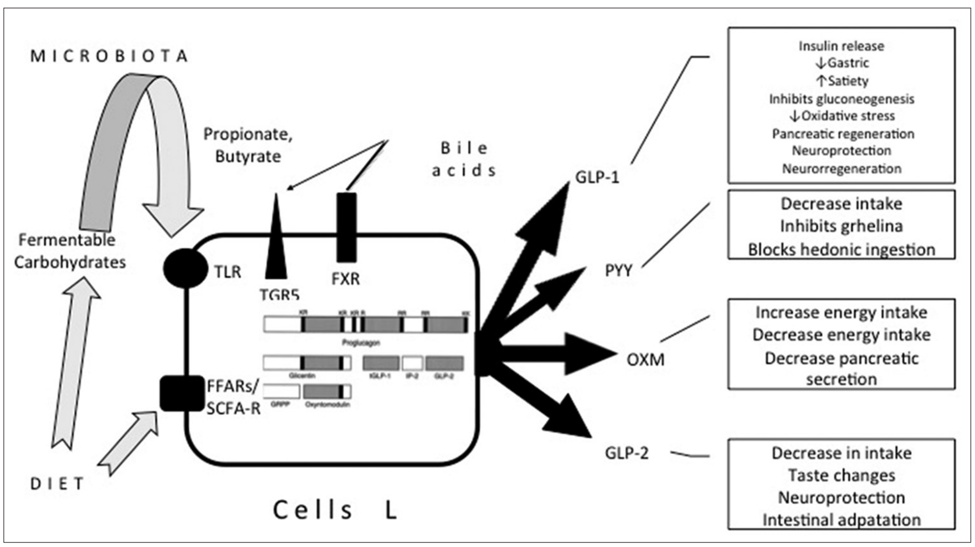


Figure 2: Microbiota of diet and L. cells

diabetic patients (1.9%) and prediabetic patients (1, 0%) while reducing or eliminating the use of oral hypoglycemic agents.[71]

Müeller-Stich *et al*. reported the results of a meta-analysis of 11 studies comparing the surgical treatment with just medical treatment and DMT2 patients in 706 patients with Grade II obesity. The reviewers concluded that metabolic (bariatric) surgery is superior to medical treatment for short-term remission of type 2 diabetes and its comorbidities. It is believed that the increased secretion of GLP-1, which results in the enhancement of insulin release stimulated by nutrients, plays an important role. Increased the production of satiety-promoting hormones, decreased the release of hunger-promoting hormones, and reduced food intake, as well as weight loss itself. In addition to the anatomically restricted caloric intake, the effect of bariatric surgery on weight loss may be related to sustained increases in the satiety-promoting intestinal hormones, such as GLP-1, GIP, and PYY, as well as reductions in factors favoring the hunger such as ghrelin.[72,73]

Fried *et al*.[10] worked with 15 adult subjects, with DMT2 treated but inadequately controlled (HbA1c of 8.0–11.0%), BMI of 27.0–40.0 kg/m^2, and peptide C ≥3 ng/mL. The follow-up was from 2 weeks and 3, 6, 9 and 12 months after the procedure of partial jejunal division (PJD). In the preclinical results, positive impacts were demonstrated with PJD in the homeostasis of glucose, cholesterol, and body composition compared to the simulated control. Clinically, PJD was successfully performed without serious complications. 12 months after surgery, the average reduction from baseline in HbA1c was 2.3% (1.3) ($P < 0.01$).[74-76]

Guilbert *et al*. last published study of this nature dates from results that included 500 patients, 83.2% women, with an average age of 38.8 years, and a BMI of 44.1 kg/m^2. The most observed comorbidities were hypertension, dyslipidemia, and diabetes. Laparoscopic gastric bypass was performed in 85.8%, gastric sleeve in 13%, and revision surgery in 1%. There were 9.8% of early complications and 12.2% of late complications, without mortality. The overall weight loss in percentage of excess weight lost at 12 and 24 months was 76.9% and 77.6%; the treatment failure was 11.4%. In patients with DMT2, there was complete remission in 68.7%, partial remission in 9.3% and improvement in 21.8% of cases. Being able to conclude that as a high volume center, bariatric surgery is safe and effective based on the low number of adverse effects and weight loss with DMT2 control.[77-79]

O'Brien *et al*.,[12] in just August of this year, reported the largest series with $n = 4023$ patients where they were followed through 4.3 years for both surgical and non-surgical patients. Bariatric surgery was associated with glycemic control, and it was established in the review of randomized trials that compared surgery versus intensive medical and lifestyle treatment of DMT2. Remission of DMT2 is common after bariatric surgery, and Roux-en-Y gastric bypass outperforms sleeve gastrectomy in most reports. More important than improvements in glycemic control is whether these glycemic changes reduce the incidence of major complications, such as microvascular events (diabetic nephropathy). Therefore, a main objective of the treatment of diabetes is to mitigate the risk of these long-term sequelae. It was previously shown that, in patients with DMT2 who have bariatric surgery, the risk of incident vascular disease is reduced by each year of remission of DMT2, even if patients eventually relapse into DMT2 (indicating an inherited effect). However, a detailed review of 2016 of the long-term microvascular results concluded that the data were a significantly lower risk of incident microvascular disease at 5 years (16.9% for surgical vs. 34.7% for non-surgical patients). Adjusted risk hazard ratio, 0.41 (95% confidence interval [CI], 0.34–0.48). Bariatric surgery was associated with a lower cumulative incidence at 5 years of diabetic neuropathy (7.2% for surgery vs. 21.4% for non-surgical patients, CRI, 0.37 [CI, 0.30–0.47]), nephropathy (4.9% for surgery vs. 10.0% for non-surgical patients: CRI, 0.41 [CI, 0.29–0.58]), and retinopathy (7.2% for surgery compared to 11.2% for non-surgical patients, CRI, 0.55 [CI, 0.42–0.73]).[80-83] The association that is intended to be carried out according to the reviewed bibliography can conclude that diabetic nephropathy responsible within the first 10 causes of mortality in our country must be attended immediately. Today, surgery is the best therapeutic element for remission of diabetes. At the same time, bipartition of intestinal transit is technically simple to reproduce and confers control to the patients submitted to this intervention, being true that there is no comparable national or international statistics on this effect in patients with diabetic nephropathy.[84-87]

Definition of the work universe and variables

Report cases, 30 cases of patients are reported, post-operated BTI, General Hospital San Juan del Rio, Querétaro. Following 1 year of his intervention (2016–2017).

Protection of people and animals and informed consent

The authors declare to carry out a study according to the World Medical Association and the Declaration of Helsinki.

Interest conflict

The authors declare that they have no conflicts of interest.

Diabetic nephropathy

The natural history of diabetic nephropathy shows a period of hyperfiltration, followed by microalbuminuria (30–300 mg/dL); subsequently, a frank proteinuria appears (>300 mg/dL). From this point, major interventions should be taken, if this does not occur, blood pressure increases, and finally renal function decreases. The presence of proteinuria is the most precocious manifestation in diabetic nephropathy, while the presence of albuminuria is a predictor of chronic renal failure. At the beginning of nephropathy, there are no significant changes, except for the increase in renal and glomerular size, due to hyperfiltration and hypertrophy.[88,89]

The hemodynamic and metabolic mechanisms as a central factor in the response to chronic hyperglycemia play a pivotal role in pathophysiology of diabetic nephropathy. Obesity and hyperglycemia directly cause vasoactive alteration, producing in the afferent and efferent arteriolar tone the increase in hyperperfusion and hyperfiltration. These early changes, as well as the changes typical of systemic hypertension, favor the development of nephropathy.[90,91]

Therefore, the aforementioned changes induce the excessive production of mitochondrial superoxide (reactive oxygen species), which activate well-established routes of cell damage, which culminate in glomerular damage, histologically characterized by thinning of the membrane basal glomerular and tubular, with increased mesangial expansion and podocytopenia [Figure 3].[92]

The potential role of GLP-1 in nephropathy is the increase of natriuresis through inhibition of the isoform 3 of the sodium-hydrogen ion exchanger in the proximal tubule (NHE3). GFR is regulated by GLP-1, conferring an antihypertensive effect, wich explains the renoprotective outcome.[93]

Experience at General Hospital San Juan del Río

Our preliminary experience was from 2016 to 2017. It is consistent with what was reported in the different

Table 1: Pre-operative demographic and biochemistry variables at 6 and 12 months			
Countable variables	**Preoperatory *n*=30 (%)**	**6 months**	**12 months**
Females, *n* (%)	16 (53)		
Age (years); average±DE (rank)	47.3±16.03 (19–76)		
Intestinal length (cm), average±DE	771±170		
DMT2 (years); average (rank)	8 (3–26)		
Dyslipidemia, *n* (%)	18 (60)		
HbA1c (%); average±DE	8.93±1.72	6.84±1.47	5.13±0.9
Triglycerides (mg/dl), average±DE	288±83	147±48.2	90.28±21.5
Total cholesterol (mg/dL), average±DE	218±20.3	135±24.39	119±20

HbA1c: Glycated hemoglobin

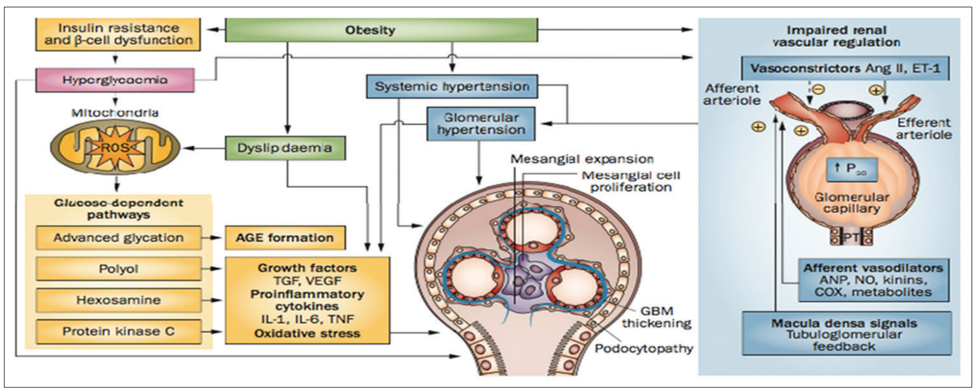


Figure 3: Adapted from doi.org/10.1038/nrneph.2013.272 4. Adapted from Muskiet *et al.*[14] AGE - Advanced glucosylation products, ANGII - angiotensin II, ANP - natriuretic atrial peptide, COX - cyclooxygenase, ET-1 - endothelin 1, GBM - glomerular basement membrane, IL - interleukin, ON - nitric oxide, P - capillary glomerular capillary pressure, PT - proximal tubule, ROS - reactive oxygen species

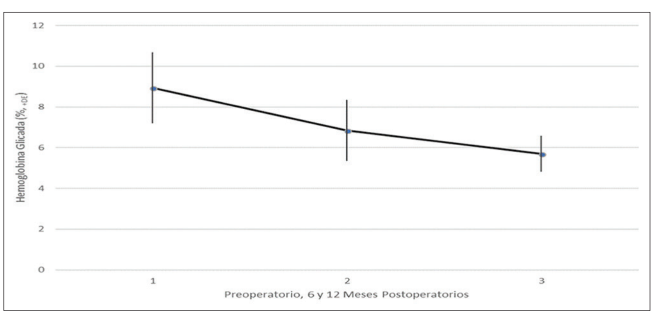
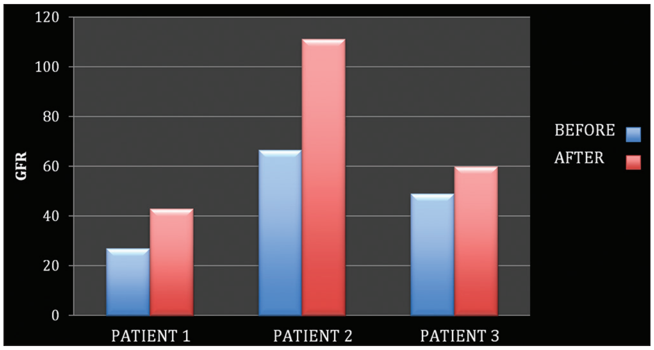


Figure 4: Pre-operative glycated hemoglobin, 6 months after surgery and 12 months of intervention

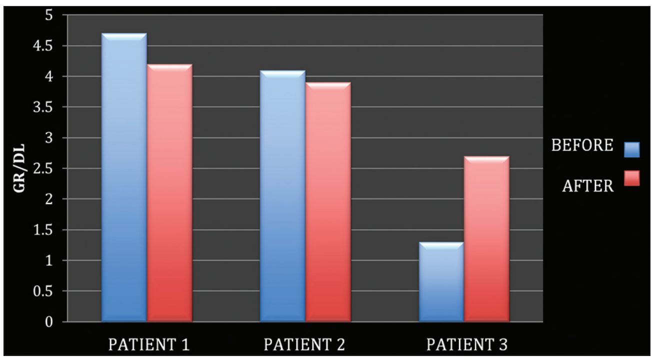
meta-analyses and multicenter studies of the US, Mexican, European and Asian counterparts.[74,80]

The sample of n = 30 is presented in Table 1, of which 16 were females (53%). The average age in years ranges from 47.3 ± 16.03 (19–76). The intestinal length in centimeters corresponds to 771 ± 170 cm. The duration of DMT2 in years was on average 8 (3–26). The total number of patients with dyslipidemia was 18 (60%). The average pre-operative glycosylated hemoglobin (%) started at 8.93 ± 1.72 at 6 months of 6.84 ± 1.47 as represented in Figure 4; and at 12 months of 5.13 ± 0.9%. Correspndingly the preoperative values of triglycerides were of 288 ± 83 mg/dl; at 6 months of 147 ± 48.2; at 12 months of 90.28 ± 21.5 mg/dL. The reported values for total cholesterol (mg/dL) started at 218 ± 20.3; at 6 months of 135 ± 24.39; and at 12 months of 119 ± 20 mg/dL.

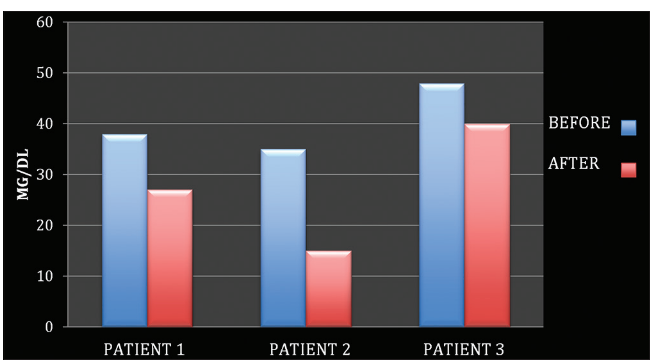
Figure 2 shows the values of GFR before and after the intervention of patient 1: 25 at 42 mL/min, patient 2: 65 at 110 mL/min, and patient 3: 45 at 60 mL/min. Likewise, Figure 3 shows excellent results, reporting the albumin value before and after the intervention in patient 1: 4.8–4.1 g/dL, patient 2: 4–3.8 g/dL, and patient 3: 1.4–2.8 g/dL. Graph 1 shows the Glomerular filtration rate that after metabolic surgery, shows better outcomes. Graph 2 shows the albumin which clearly improves after intervention. Graph 3 shows the blood ureic nitrogen where toxicity before surgery was documented, after metabolic surgery decrease continuously. Graph 4: Creatinine value started to filtrated with better performance, due to



Graph 1: Glomerular filtration rate before (blue) of intestinal bipartition surgery and 1 year follow-up (2016–2017) (red). Electronic clinical record, San Juan del Río General Hospital, Queretaro

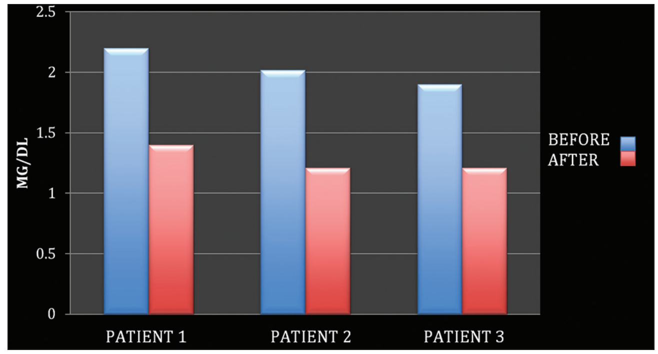


Graph 2: Albumin value before (blue) of intestinal bipartition surgery and 1 year follow-up (2016–2017) (red). Electronic clinical record, San Juan del Río General Hospital, Queretaro

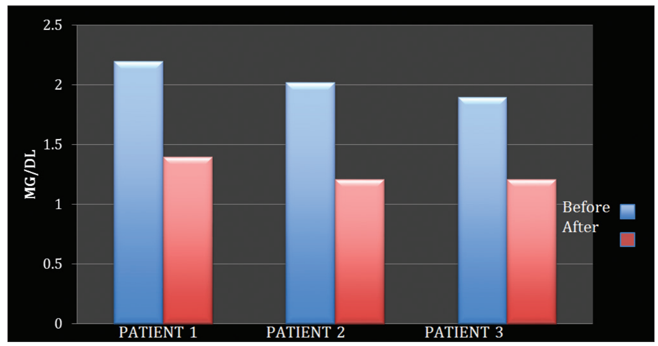


Graph 3: Blood ureic nitrogen value before (blue) of intestinal bipartition surgery and 1 year follow-up (2016–2017) (red). Electronic clinical record, San Juan del Río General Hospital, Queretaro

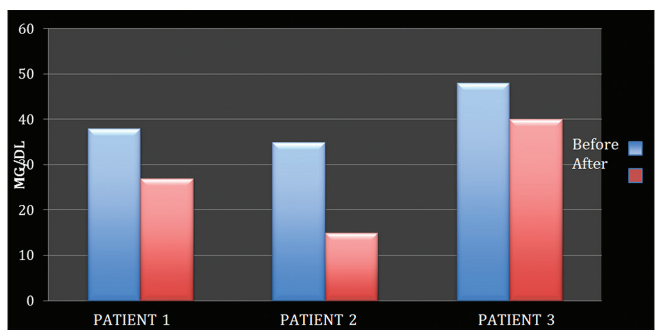
biochemistry addpatation process. Graph 5 shows the blood urea nitrogen value (BUN), before and after the intervention in patient 1: 39–28 mg/dL, patient 2: 35–15 mg/dL, and patient 3: 49 a 40 mg/dL. Finally, Graph 6 presents the incredibly reported value of creatinine that was achieved before and after the intervention of patient 1: 2.3–1.4 mg/dL, patient 2: 2–1.2 mg/dL, and patient 3: 1.9–1.2 mg/dL.



Graph 4: Creatinine value before (blue) of intestinal bipartition surgery and 1 year follow-up (2016–2017) (red). Electronic clinical record, San Juan del Río General Hospital, Queretaro



Graph 5: Blood Ureic Nitrogen Value [BUN] before (blue) of Intestinal Bipartition Surgery and one year follow-up [2016-2017] (red). Electronic clinical record, San Juan del Río General Hospital, Queretaro.



Graph 6: Creatinine value before (blue) of Intestinal Bipartition Surgery and one year follow-up [2016-2017] (red). Electronic clinical record, San Juan del Río General Hospital, Queretaro.

General recommendations that are proposed from the study are: Do not DE functionalize more than 2/3 parts of the intestine if there is transanastomotic preferential passage.[75] Allow a minimum of 100 cm of intestinal length in case a transanastomotic preferential passage was created, which we consider inappropriate, in principle, to standardize the site of the anastomosis.[76,77] It is noteworthy that preliminary study of patients is frankly heterogeneous and a small sample, so it is necessary to follow up on subsequent years with an increase in the number of cases, to show the results proposed internationally.[72,73,78,79,81]

As previously discussed, it is not suggested that there is <30% bipartition due to the high probability of dysbiosis.[75]

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CONCLUSION

The surgical intervention evidenced the metabolic effects of reducing the jejunum and visceral fat (omentectomy), being statistically significant the benefits found in patients with DMT2 obesity Grade II and normal weight. Likewise, there are no obstacles to food intake, without prosthesis, without excluded segment, and without malabsorption. The general structure and function of the digestive tract are maintained with this surgery. GLP-1 and its secretion together with PYY are elevated, while laboratory tests preoperatively, at 6 months, and 12 months benefit.[68,71,82]

Finally, in long term, the treatment with bipartition of intestinal transit promoting GLP-1 protects the kidney and preserves, as well as the increase of the GFR. The inactivation of the isoform 3 (NHE3) exchanger results in the significant decrease in reactive free oxygen species.

This surgery based on the neuroendocrine brake principle is safe and a potentially effective option in the management of patients with DMT2 and diabetic nephropathy.[3-5,18,29,70,84]

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