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BP Limb Length as a Factor for T2DM Remission

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ABSTRACT

Background: There has been increased interest in identifying the associated factors to Type 2 Diabetes Mellitus (T2DM) remission after bariatric surgery. One of these factors is the BP limb length. The objective of our study was to evaluate the T2DM remission rate in patients subjected to Roux -en- Y gastric bypass (RYGB) who had different Biliopancreatic (BP) limbs length.

Methods: 48 patients with obesity grade II, and T2DM diagnosis, were subjected to RYGB and completed a one year of surgical follow up. All patients were grouped according to the BP limb length: In group A (n= 24) patients with BP limbs of 100 cm or less; in group B (n= 24) patients with BP limb from 150 to 170 cm in length.

Results: Both groups presented an elevated remission rate of T2DM (83% full remission in the population studied). In group A 18 patients (75%) presented a full remission, while 2 patients (8.3%) showed a partial remission and only 4 patients (16.7%) were considered without remission at the one year follow up. In group B all patients had some remission: 22 patients (91.7%) presented a full remission (91.7%) and the rest of the patients showed a partial remission (8.3%), no significant difference was found between the two groups.

Conclusions: Bariatric surgery remains as the best long term treatment for obesity and its comorbidities, despite some differences in the RYGB technique, BP limb length from 50 to 170 cm did not affect post RYGB glycemic control.

KEYWORDS: Bariatric surgery, Biliopancreatic limb length, type 2 diabetes mellitus, Roux-en-Y gastric bypass.

ARTICLE DETAILS

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INTRODUCTION

Obesity is a pathological condition whose prevalence has increased worldwide in the last 50 years. In 2016, 39 % of adults at world level were overweight and 13 % were obese; while in 2018, 75.2 % of the Mexican population fit in one of those categories[1]. Obesity increases the risk of developing chronic diseases in which Type 2 Diabetes Mellitus (T2DM) stands out, due to the fact that 18 to 20% of patients with obesity are also diabetic[2].

With the use of treatments for T2DM, such as drastic lifestyle changes and pharmacological measures, a remission rate of 15 % has been reported[3]. However bariatric surgery has proven to be an effective long-term treatment for the attached comorbidities, having a main impact on T2DM. Remission rates for T2DM have been reported from 58.2% at 2 years, and 46.6% at 5 years after bariatric surgery. Also, an increase in quality and life expectancy have been observed[4].

One of the main surgical procedures performed for obesity management and its comorbidities is the Roux-en-Y gastric

bypass (RYGB), which has been considered historically as the best surgical treatment to maintain a weight reduction and comorbidities control on a long term basis[5].

When a RYGB is executed, a gastric remnant or "pouch" is developed of approximately 30 mL from the proximal stomach, in which an anastomosis with an intestine handle is performed in order to form the feeding limb, which can have from 75 to 150 cm of length. Additionally, to those the biliopancreatic (BP) limb is anastomosed to create a common end. The BP limb usually has a length of 50 to 150 cm. It is considered that the common limb should be longer than 200 cm, to enable a sufficient nutrient absorption to prevent malnutrition[6].

Currently, there has been increased interest in identifying the associated factors to the glycemic control and subsequent T2DM remission after bariatric surgery, such as preoperative weight, preoperative glucose level or insulin use. One of these factors is the BP limb length. It has been reported that, the more distal is the food first point of contact with the small intestine mucosa, the sensibility to both insulin and glycemic control is better, supported by comparing the glycemic excursion after the direct nutrients infusion into the duodenum, the proximal jejunum or the medial jejunum in T2DM patients[7].

On the other hand, other studies have obtained T2DM remission rates with shorter BP limbs (31.2%), comparable to those obtained with longer ones (37.5%)(8). Even in gastric sleeve post-surgical patients, remission rates in T2DM from up to 56.29%, despite the fact that it is a purely restrictive procedure in which there is no BP limb, and just the total stomach volume is reduced[9].

In the sight of that, the objective of our study was to evaluate the T2DM remission rate in patients subjected to RYGB who had BP limbs longer than 100 cm compared to those who had shorter ones.

METHODS

Subjects

A retrospective cohort from 2013 to 2019, in which we included 48 patients with obesity grade II (considered as a Body Mass Index (BMI) over 35 kg/m^2) and T2DM diagnosis, defined as HbA1c over 6.5% or an fasting blood glucose equal or over to 126 mg/dL in two separated measures, who were subjected to RYGB and completed a one year of surgical follow up in University Hospital "Juan I. Menchaca", Guadalajara, Mexico. All patients were grouped according to the BP limb length: in group A (n= 24) patients with BP limbs with 100 cm or less in length; in group B (n= 24) patients with BP handles from 150 to 170 cm in length. There were no patients with BP handles of 101 to 149 cm. The investigation was approved by the Ethics Committee from University Hospital "Juan I. Menchaca" (approval number: 00036).

Both groups had the following variables analyzed before the surgery: age, sex, BMI at the start of the program, BMI lost before the surgery, pre-surgical weight, years with T2DM before the surgery, oral hypoglycemic agents (OHAs) use, insulin use, fasting blood glucose was analyzed using Beckman Coulter AU5800 equipment, pre-surgical HbA1c was measured using BIORAD D10, serum insulin was analyzed using DX1800 chemo-luminescence process and C-peptide using Diasorin LiasonX equipment.

T2DM remission was considered in patients who presented HbA1C levels below 5.7% a year after the surgery, without the need of pharmacological treatment or insulin; also, it was considered as partial remission if patients had HbA1c between 5.7 and 6.4%, and without remission if the HbA1c was equal or over 6.5%[8].

Statistical analysis

Spearman correlation was used to determine the correlation between the BP limb length and the HbA1C levels decrease after one year of the surgery. For the group comparison, Mann-Whitney U-test, Wilcoxon test and Chi-squared test were used. The statistical analysis was performed using IBM SPSS Statistics for Windows version 27 (IBM Corp., Armonk, NY, USA). Difference in variables analyzed or correlations were considered significant if $p < 0.05$.

RESULTS

Demographic and clinical pre-surgical characteristics

The demographic and clinical pre-surgical characteristics of all the participants are described in Table 1. In relation to age, weight, pre-surgical BMI, and BMI loss, both groups were similar (p= 0.556, p= 0.138, p= 0.529 and p= 0.828, respectively). However, group A had fewer female subjects compared to group B ($p < 0.05$).

In relation to the biochemical variables related to T2DM, no significant differences were found in glucose levels, HbA1c, time living with T2DM, and insulin use prior to surgery (p= 0.322, p= 0.16, p= 0.12, p= 0.081 respectively). Nevertheless, it was observed that group B (long BP limb) presented higher levels of serum insulin ($p < 0.05$) and C-peptide ($p < 0.001$) (Table 1).

Clinical post-surgical characteristics and remission of T2DM

Table 2 shows all the post-surgical parameters evaluated. A year after the surgery, all patients presented an important decrease in weight, BMI and Hba1C, regardless of the BP limb length. Nevertheless, group B participants had a greater weight loss in comparison to group A ($p < 0.05$). Both groups presented an elevated remission rate of T2DM (83% full remission in the population studied). In detail, in the group A, 18 patients (75%) presented a full remission, while 2 patients (8.3%) presented a partial remission and only 4 patients (16.7%) were considered without remission at the one year follow up. Furthermore, in the group B all patients had some remission: 22 patients (91.7%) had a full remission, and the rest of the patients showed a partial remission (8.3%) (Figure 1); it is worth noticing that in the moment of the remission

evaluation none of the patients were under OHAs or insulin treatment. However, no significant difference was found between the two groups (p= 0.111). Additionally, there was a significant decrease of Hba1c levels ($p < 0.001$, in both groups) in the one-year follow-up after the surgery independently of the length of the BP limb.

In this study, biliopancreatic limb length showed no correlation with HbA1c levels at one year follow-up (p= 0.644, Rho= 0.068); however, it did show low negative correlation with postoperative weight and BMI, one year after the surgery ($p < 0.05$, Rho- 0.329 and $p < 0.05$, Rho= -0.318, respectively) (Figure 2).

On the other hand, a low positive correlation was found between the evolution years with T2DM and HbA1c at one year follow-up ($p < 0.05$, Rho= 0.310). In addition, a low positive correlation was found between age and postoperative HbA1c ($p < 0.05$, Rho= 0.307). Also, no correlation was found between preoperative HbA1c and postoperative weight and BMI (p= 0.347, Rho=0.139, and p= 0.976, Rho=0.004, respectively).Finally, no mortality was reported in any of both groups.

DISCUSSION

Bariatric surgery continues to be an effective treatment for morbid obesity control. Also, in an important percentage of patients it can also induce a remission of the associated comorbidities, mainly T2DM. Regardless of the performed technique specifics, there is a high percentage of patients that achieve an adequate metabolic control, reflected by a serum glucose decrease as well as the HbA1c, without the need for OHAs and insulin[10].

In the randomized assay performed by Homa J et al. the effect of the length of the BP limb (150 cm vs 75 cm) was compared over the weight loss of the patients that went into RYGB. In that investigation, they concluded that patients with longer BP limbs managed a significantly higher weight loss during the first year after the surgery; however, this difference between the groups was not significant in the four years follow-up[11]. On the other hand, in a retrospective study there were no significant differences in weight loss when the post-surgical parameters were compared after a year for 46 patients that underwent RYGB with BP limb of 60 cm vs 43 patients with BP limb of 150 cm. Specifically, 35 patients had a pre-surgical diagnosis of T2DM; in addition, 75% of the diabetic patients of the long BP limb presented remission when compared with 50% of the patients with regular BP limb (60 cm), however, these results did not show any statistical significance (p= 0.37)[12].

These findings are similar to the ones found in our study, regardless that the remission percentage was higher in the long BP limb patients' group; nevertheless, a significant difference was not proven in order to allow us to recommend longer limb in patients with T2DM as a routine measure. Also, similar results were found in this study regarding weight loss, long BP limb group resulted in a significantly lower postoperative weight compared with the short limb BP group.

Nora M, et al. performed a cohort study with the objective of determining the relationship between the BP limb length with T2DM remission. This study included 41 patients to which a standard RYGB with a BP limb of 84 cm in average was performed, compared to a group of 73 patients with a BP limb of 200 cm and a five year follow up. They observed both the percentage of weight loss (73% vs 65%, $p < 0.05$) and the remission rate of T2DM (73% against 55%, $p < 0.05$) in patients with long BP limb. Whereby they concluded that a RYGB with a BP limb of 200 cm is associated with a higher remission rate, a lower percentage of relapse into the disease and a lower necessity of anti-diabetic drugs in those patients with persistent diabetes[13].

The mechanisms for which the T2DM remission is produced are complex. The sensibilization to insulin, the beta pancreatic cells function and the complicated interaction between hormones in the entero-insular axis seem to play an important role through different mechanisms by which, just one factor, in this case the length of the BP limb, cannot determinate by itself if the patients manage to achieve an adequate remission or not[10].

Additionally, there are other factors that seem to intervene in the patient prognosis, such as the years with T2DM before the surgery. In our study, this parameter showed to be a determinant factor since those patients with more years of evolution had lower T2DM remission rates ($p < 0.05$, Rho= 0.310). Age at the moment of surgery also seems to play an important role in the process for glycemic control after surgery, this suggests that actions to promote bariatric surgery in earlier stages of life will result in better results regarding glycemic control in diabetic patients, as demonstrated in this study.

It is worth mentioning that longer BP limbs can also be associated with a higher vitamin and iron deficit as mentioned in Ruiz J, et al. In a randomized clinical assay of 250 patients with 5 years follow up, in which the effects of a BP limb of 70 cm against 120 cm were compared, using a 150 cm feeding limb in both cases. It was observed that the RYGB with a 120 cm BP limb cannot manage a higher weight loss or comorbidities remission compared to the shorter one, however the longer limb was associated with a higher deficiency of B12 and A vitamins and folic acid, this could play an important role in the decision making process when selecting and planning the surgery for each patient[14].

In conclusion, bariatric surgery is a safe and effective treatment option for both obesity and diabetes, as demonstrated in this study in which both study groups presented a high remission percentage of T2DM, however no significant difference was found between both groups by which we could infer that the BP limb length is not related with T2DM remission. Group B (long BP limb) presented less post-surgical weight with 72 kg (61.7 - 87.35) compared to group A (short BP limb) which presented 84.5 kg (76.88 -

94.7), such variable was not significant regarding the remission rate of the patients. Group B (long BP limb) presented a lower post-surgical BMI with 27 compared to group A (short BP limb) which presented a BMI of 30, such variable was not significant to predict T2DM remission rate. Both groups showed an improvement in Hba1c levels after the surgery.

The full remission rate in group B was 91.7% of the cases while in group A only 75% had a full remission, the higher number of patients without remission was found in group A (short BP limb).

The higher remission rate was presented in those patients whose diagnosis of T2DM had an evolution period from 1 to 5 years.

Regarding age, the 26 - 45 age group had a higher rate of full remission, it is worth noticing that in this same group the higher number of patients without remission is also shown.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

JAAO, MPSM designed the study. MPSM supervised the study. JAAO, AREY and MdRRB analyzed the data and wrote the manuscript. Surgical teams who performed all surgeries were integrated by MPSM, CRLL, VMNN, CMMM, FPJZ and LMFC. MSAA supervised the ethical aspects and psychological well-being of patients. All authors reviewed critically and approved the definitive version of the manuscript to be published.

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Table 1. Demographic and clinical pre-surgical characteristics of participants

Variable	Group A (short BP limb) (n= 24)	Group B (long BP limb) (n= 24)	*p* value
Sex, N (%)			
Female	15 (62.5)	22 (91.7)	*< 0.05*[a]
Male	9 (37.5)	2 (8.3)	
Age, years; median (IQR)	43 (38 - 51.75)	42.5 (36.5 - 47)	0.556[b]
Weight, kg; median (IQR)	120.3 (105.2 - 138.8)	105.33 (95.4 - 129.75)	0.138 [b]
BMI, kg/m^2; median (IQR)	44.15 (37 - 45.7)	40.75 (35.83 - 46.75)	0.529 [b]
BMI lost, kg/m^2; median (IQR)	2.0 (0.9 - 2.95)	1.65 (1.2 - 3.35)	0.828 [b]
Glucose, mg/dL; median (IQR)	103 (82.7 - 130)	108.5 (93 - 134.5)	0.322 [b]
HbA1c, %; median (IQR)	6.55 (5.9 - 7.3)	6.85 (6.43 - 7.38)	0.16 [b]
Insulin, uU/mL; median (IQR)	18.75 (11.7 - 26.65)	23.55 (21.93 - 36.88)	*< 0.05* [b]
C Peptide, (ng/mL); median (IQR)	3.45 (2.93 - 3.9)	4.83 (3.9 - 5.18)	*< 0.001* [b]
Time with T2DM, years; median (IQR)	2.75 (1 - 5.38)	1.5 (0.8 - 2.4)	0.12 [b]
OHAs use, N (%)			0.391 [a]
0	5 (20.8)	5 (20.8)	
1	12 (50)	16 (66.7)	
2	6 (25)	3 (12.5)	
3	1 (4.2)	-	
Insulin use, N (%)	5 (20.8)	1 (4.2)	0.081 [a]

[a] Chi square test,

[b] Mann-Whitney U-test

Table 2. Pre- and post-surgical parameters evaluated in all participants.

Variable	Group A (short BP limb) (n= 24)	Group B (long BP limb) (n= 24)	*p* value
Pre-surgical weight, Kg; median (IQR)	122.7 (105.25 – 138.88)	111 (95.4 – 129.75	0.138[b]
Post-surgical weight, Kg; median (IQR)	86.37 (76.88 - 94.7)	74.41 (61.7 - 87.35)	*0.019* [b]
Pre-surgical BMI, Kg/m^2; median (IQR)	42.63 (37.03 – 45.7)	41.49 (35.83 – 46.75)	*0.529* [b]
Post-surgical BMI, Kg/m^2; median (IQR)	30.08 (26.8 - 31.8)	27.62 (24.35 - 30.5)	0.069 [b]
Pre-surgical HbA1c, %, median (IQR)	6.76 (5.93 – 7.35)	6.7 (6.43 – 7.38)	0.160 [b]
Post-surgical HbA1c, %; median (IQR)	5.55 (5.13 - 5.68)	5.34 (5.03 - 5.6)	0.379 [b]
T2DM Remission			
Full	18 (75.0%)	22 (91.7%)	0.111[a]
Partial	2 (8.3%)	2 (8.3%)	
Without remission	4 (16.7%)	0 (0%)	

[a] Chi square test,

[b] Mann-Whitney U-test

FIGURES

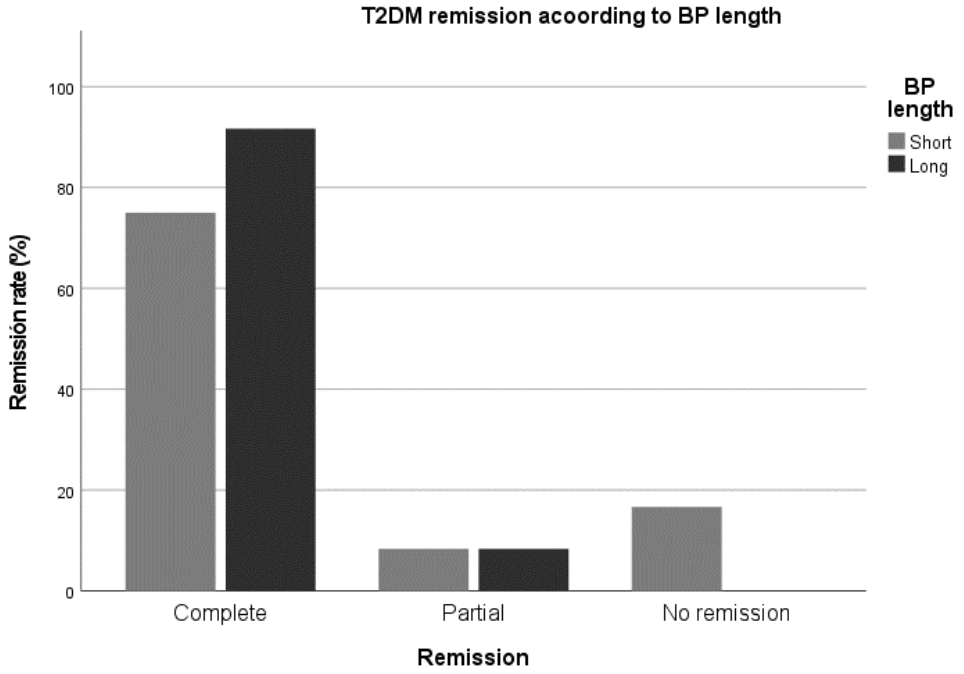

Figure 1. T2DM remission rate according to the length of BP limb.

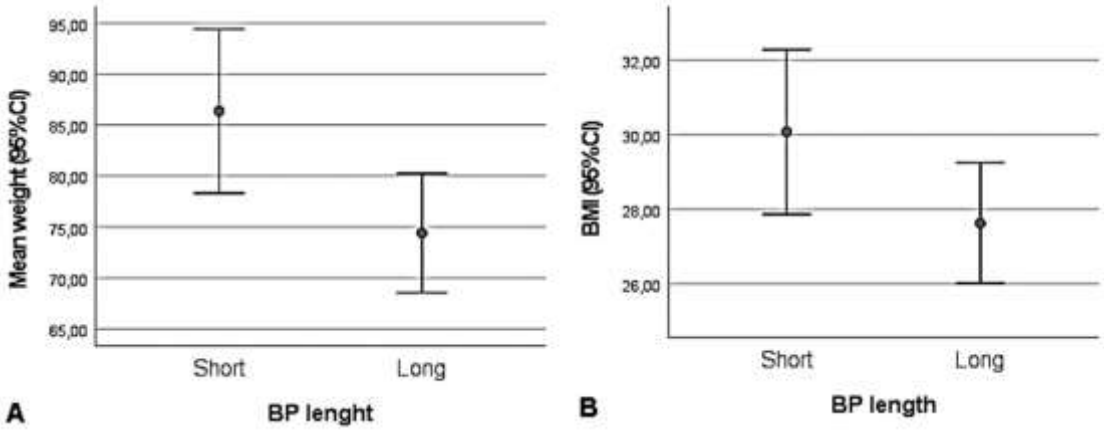

Figure 2. Error bar graph of the correlation between BP length and Weight (A), and the correlation between BP length and BMI (B).

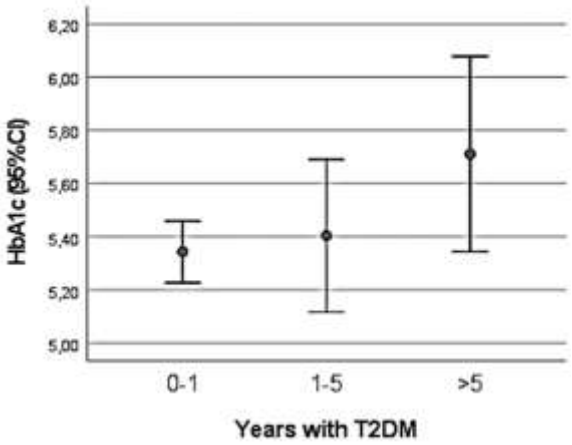

Figure 3. Error bar graph of the correlation between years with T2DM and postoperative HbA1c