PROGNOSTIC FACTORS AND PATHOPHYSIOLOGY OF DIABETES REMISSION AFTER METABOLIC GASTRIC BYPASS, SLEEVE GASTRECTOMY AND GREATER CURVATURE PLICATION: A RANDOMIZED CONTROLLED TRIAL

Vilarrasa Núria [1,5], Casajoana Anna [2], García Ruiz de Gordejuela Amador[2], Pujol Jordi[2], Duran Xavier[3,5], Garrido Pilar[4], Monseny Rosa[4], Vendrell Joan[3,5], Fernandez Veledo Sonia[3,5].

[1] Endocrinology Unit. Bellvitge University Hospital-IDIBELL, Barcelona, Spain[2]General Surgery and Obesity Unit, Bellvitge University Hospital-IDIBELL, Barcelona, Spain
[3]Hospital Universitari de Tarragona Joan XXIII, Institut Investigació Sanitaria Pere Virgili, Universitat Rovira i Virgili
[4]Clinical Nutrition Unit. Bellvitge's University Hospital-IDIBELL, Barcelona, Spain
[5]CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Bellvitge University Hospital-IDIBELL

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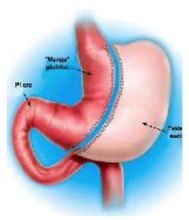
INTRODUCTION

Thirty-nine percent of morbidly obese patients have type 2 diabetes mellitus (T2DM) and 80% of them can achieve diabetes remission after bariatric surgery. However, there are few randomized studies comparing the metabolic results of different surgical techniques and the hormonal mechanisms involved. There are several factors related to diabetes improvement after bariatric surgery (BS), among which outstands weight loss (WL), decreased caloric intake, intestinal malabsorption, changes in biliopancreatic salts, and in gut hormones, particularly those implicated in the incretin axis. The influence of each of these factors might vary with the surgical technique and their respective anatomical modifications. By-passing the duodenum provokes an increase in GLP-1 that has been associated to glucose improvement and gastric fundus exclusion causes a reduction in the secretion of the Ghrelin orexigen hormone.

Metabolic Gastric Bypass (mGBP)

Sleeve Gastrectomy (SG)



Greater Curvature Plication (GCP)

OBJECTIVES

To study and compare the improvement of T2DM and the hormonal pathways following three surgical techniques: metabolic gastric bypass (mGBP), sleeve gastrectomy (SG) and greater curvature plication (GCP).

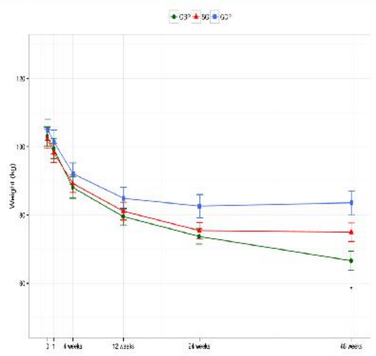
METHODS

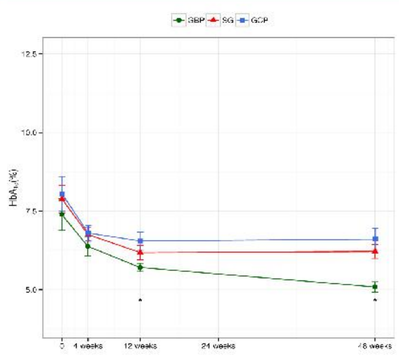
Prospective, randomized controlled single-center study in patients with T2DM and morbid obesity. 45 patients were randomly assigned (1:1:1) to the 3 surgical techniques. (Trial registration ISRCTN: 14104758). At baseline, one and 12 months a standard meal test was performed to determine GLP-1, GLP-2, PYY, Ghrelin and glucagon concentrations. GLP-1 was measured by radioimmunoassay (Millipore, Saint Charles, MO). Glucagon and PYY by enzyme immunoassay (Yanahaira Institute Inc., Awakura, Japan). Plasma ghrelin was determined by enzyme immunoassay (CUSABIO, Wuhan Hi-tech Medical Devices, China).

Table1.**- Initial Characteristics of patients**

	mGBP (n=15)	SG (n=15)	GCP (n=15)	*p*
Sex H/D	7/8	5/10	3/12	0.301
Age (year)	51.10±7.70	49.20±9.16	49.70±8.12	0.827
Weight (Kg)	103±10.8	102±10.8	105±12	0.907
BMI (Kg/m^2)	38.7±2.01	39.0±1.68	40.7±1.34	*0.010*
Waist circumference (cm)	118.87±7.58	117.53±7.56	117.33±8.95	0.882
Total adipose tissue (%)	37.58±7.80	37.91±5.05	36.36±11.91	0.989
T2DM duration (months)	54 [39.5;114]	120 [51.2;180]	83 [45;144]	0.216
C- Peptide (ng/ml)	3.04 ±1.01	3.13 ±1.80	3.75 ±2.75	0.566
Fasting glucose (mmol/L)	8.38±3,00	9.55±3.57	9.84±5,25	0.566
HbA1c (%)	7.39±1.95	7.89±1.71	8.05±2.15	0.498
T2DM treatment [%, (n)]				
Metformin	100 (n=15)	93.3 (n=14)	80 (n=12)	0.302
Sulfunilurea	20 (n=3)	13.3 (n=2)	40 (n=6)	0.311
GLP-1 analog	20 (n=3)	20 (n=3)	26.70 (n=4)	1.000
DPP-IV inhibitor	26.70 (n=4)	40 (n=6)	6.67 (n=1)	0.130
Insulin treatment [%, (n)]	33.30 (n=5)	40 (n=6)	40 (n=6)	0.910
Insulin total dose (UI/day)	73.20 [21-102]	86.67 [16-142]	79.71 [10-164]	0.835
Insulin dose/Kg/day	0.72±0.34	0.84±0.45	0.78±0.60	0.751
Dyslipidemia (%, n)	73.3 (n=11)	80 (n=12)	86.7 (n=13)	0.894
High blood pressure (%, n)	66.7 (n=10)	73.3 (n=11)	80 (n=12)	0.912

RESULTS





*p<0.05 between GBP compared to SG and GCP

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- ✓ After bariatric surgery (BS), total weight loss was higher at 24 and 48 weeks in mGBP compared with SG and GCP (Figure 1). HbA_{1c} was significantly lower in mGBP at 12, 24 and 48 weeks compared with SG and GCP (figure 2).
- ✓ AUC for plasma glucose was significantly lower in mGBP at one and 12 months (figure 3). AUC for GLP-1 and GLP-2 increased significantly at one and 12 months after mGBP (figures 4-5); at 12 month fasting concentrations of PYY and ghrelin increased after mGBP (figures 6, 8).

	Total remission	Partial remission	Non-remission	p
MGBP (n,%)	12 (80%)	3 (20%)	0 (0,0%)	<0.001
SG (n,%)	8 (53.3%)	1 (6.67%)	6 (40%)	
GCP (n,%)	3 (20%)	4 (26.7%)	8 (53.3%)	
Basal HbA_{1c} (%) <6	5 (83.3%)	0 (0%)	1 (16.7%)	<0.001
6-6,5	8 (88.9%)	1 (11.1%)	0 (0%)	
>6.5	10 (33.3%)	7 (23.3%)	13 (43.3%)	
Diabetes duration (month)	77 [43.5-114]	47 [31.2-66.5]	160 [105-230]	0,004
C-Peptide $_{b\ (ng/ml)}$	1.56 [1.32-2.13]	1.92 [1.80-2.40]	2.10 [1.53-2.61]	0.472
Insulin treatment Yes	4 (23.5%)	3 (17.6%)	10 (58.8%)	0,003
Not	19 (67.9%)	5 (17.9%)	4 (14.3%)	
Insulin (UI/Kg/day)	0.52 [0.17-0.92]	0.73 [0.42-0.74]	0.95 [0.67-1.16]	0.115
WL $_{b\text{-}12\ month}$	-30.10 [-36.42;-25.84]	-31.75 [-33.35;-22.08]	-22.00 [-26.80:-17.30]	0.007
AUC GLP-1 $_{1m\text{-}b}$	140[43.7;214]	23.3[-7.80;75.7]	7.24[-31.8;40.2]	0.001
AUC GLP-2 $_{1m\text{-}b}$	67.3[24.8;118]	19.5[8.47;39.9]	23.1[7.26;40.0]	0.009

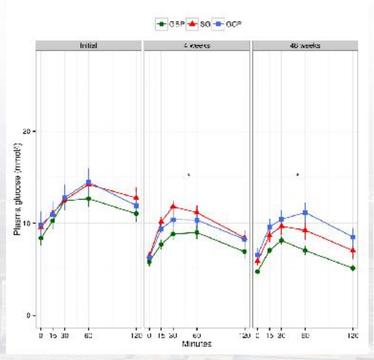

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Figure 3- AUC for glucose after BS.

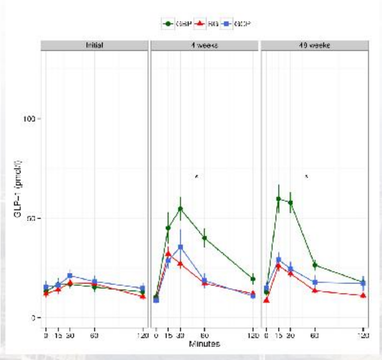

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Figure 4- AUC for GLP-1 after BS.

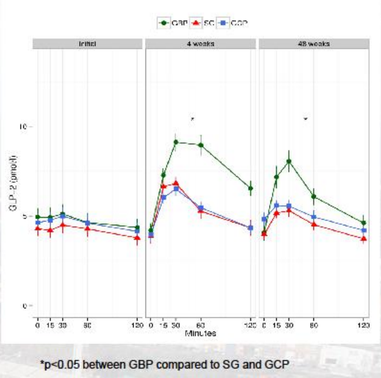

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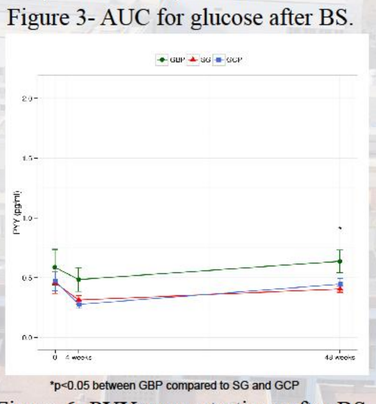
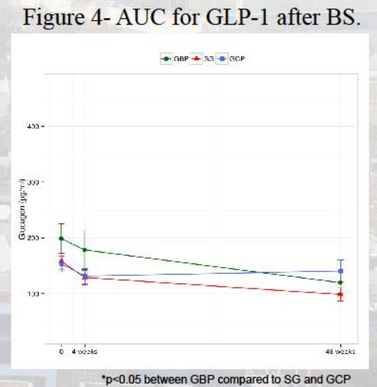
Figure 5-AUC for GLP-2 after BS.



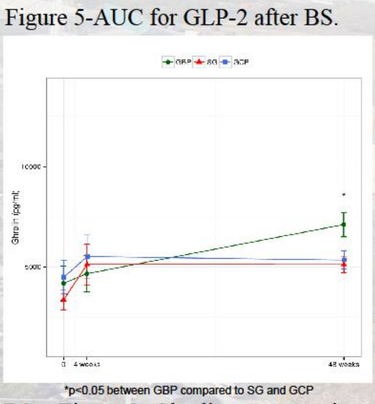
*p<0.05 between GBP compared to SG and GCP

Figure 6- PYY concentrations after BS.



*p<0.05 between GBP compared to SG and GCP

Figure 7- Glucagon concentrations after BS.



*p<0.05 between GBP compared to SG and GCP

Figure 8- Ghrelin concentrations after BS.

- ✓ Multiple logistic regression analysis showed a negative association between probability of T2DM remission and insulin treatment (ß-3.67, OR 0.025, p= 0.018), and a positive association with higher increase in ΔAUC GLP-1 at month one after BS (ß 0.021, OD 1.021, p= 0.013).
- ✓ No correlation was found between changes in Ghrelin, PYY and glucagon or WL and DM remission.

CONCLUSIONS

- ✓ mGBP is the technique that has shown a higher rate of weight loss and T2DM remission compared to SG and GCP.
- ✓ Factors associated with improved glycemic control are those that accompany a less evolved diabetes being the most important the absence of insulin treatment.
- ✓ Regarding hormonal pathways, an enhanced secretion of GLP-1 was associated with a higher rate of T2DM remission.

Generalitat de Catalunya Departament de Salut
Institut Català de la Salut Gerència Territorial Metropolitana Sud
Bellvitge Hospital Universitari
IDIBELL Institut d'Investigació Biomèdica de Bellvitge
Universitat de Barcelona

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