10 YEARS OF BREAKTHROUGHS A HEALTHIER FUTURE

DIRECT
DIABETES RESEARCH ON PATIENT STRATIFICATION

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Glucagon and incretin hormones changes after Roux-en-Y gastric bypass

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Facts & Figures

Start date	01/02/2012
End date	31/07/2019
Contributions	
IMI funding:	21 388 643 €
EFPIA in kind:	18 816 527 €
Other:	6 479 086 €
Total Cost:	46 684 256 €
Project website:	www.direct-diabetes.org
Social media:	Facebook, Twitter

Challenge

The most effective treatment for obesity in terms of weight loss and comorbidity resolution is Roux-en-Y gastric bypass (RYGB) and has been proven superior to the medical treatments available for diabetes management and obesity. The mechanisms behind the long lasting weight reduction and T2D remission after surgery are still unclear. It has been hypothesized that the changes of circulating levels of gut hormones, in particular incretins hormones, are essential for this outcome. With this study, we aimed to assess the postprandial changes of the incretin hormones in obese patients with T2D that underwent to RYGB.

Approach & Methodology

- Mixed meal tests were performed in 39 patients before and 3 months after surgery. Blood samples were taken at baseline and 15, 30, 60, 90, 120 and 180 minutes after ingestion of a standardized mixed meal test.
- RYGB were performed by laparoscopy at the University of Lille.
- Blood samples for incretins analyses were collected into vacutainers containing a proprietary cocktail of protease inhibitors (P800 tubes, Becton-Dickinson). Resulting P800 plasma was then used for quantification of incretin hormones by immunoassays at Sanofi Frankfurt.
- Areas under the curve were calculated as the total area (T-AUC) and area above baseline (I-AUC) using the trapezoidal method. Statistical analysis were performed using the Wilcoxon signed rank test in order to compare the results before and after RYGB.

Results

We showed how the RYGB surgery changes the dynamic of the meal response of glucose, insulin and C-peptide. Moreover, we observed higher levels of postprandial GLP1, GIP, PYY and Glucagon three months after bariatric surgery.

	Preoperative values	Postoperative values	p value
Men/Woman	16/23	16/23	-
Age (years)	51.8(±7.4)	51.8(±7.4)	-
Weight (kg)	126(±19.6)	105.6(±15.5)	$7.7x10^{-8}$
BMI (kg/m²)	44.6(±6.1)	37.5(±5.3)	$7.7x10^{-8}$
Fasting plasma glucose (mmol/L)	8.8(±3.3)	5.9(±1.8)	$2.8x10^{-6}$
Fasting plasma insulin (pmol/L)	28.3(±40.2)	10.6(±6.6)	$41.4x10^{-6}$
Fasting C-peptide (ng/mL)	4.3(±1.8)	3.5(±1.2)	0.008
HbA1c (%)	7.3(±1.6)	6.1(±1.0)	$3.8x10^{-7}$

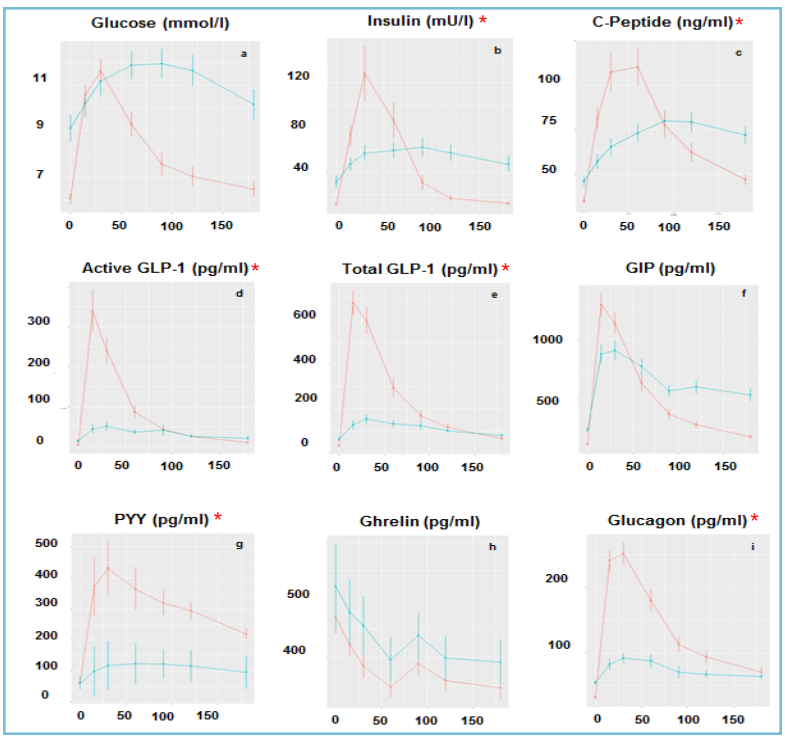

Fig 1. Mean Curves with SEM. The colors illustrate preoperative (blue line) and postoperative data (red line); x axis represents the time in minutes. *statistically significant AUC difference.

Value of IMI collaboration

This collaboration allowed to share scientific knowledges, samples, data, and technical skills across the members of this study.

Impact & take home message

Understand the biological mechanisms behind the T2D remission after surgery is important to develop new drugs for a less invasive treatment of diabetes.

This work has received support from the EU/EFPIA/ [FP7/2007-2013] Innovative Medicines Initiative [2] Joint Undertaking DIRECT grant no 115317.