

INTERNATIONAL CONFERENCE ON GASTROINTESTINAL SURGERY TO TREAT TYPE 2 DIABETES

Clinical and Research Guidelines Development

**Rome, Italy
March 29-31, 2007**



DSS
DIABETES SURGERY SUMMIT



**Auditorium
Università Cattolica
del Sacro Cuore
Rome, Italy**



DIABETES SURGERY SUMMIT

Clinical and Research Guidelines Development

With the High Patronage of
the President of the Italian Republic

Under the Auspices of
European Commission for Health and Consumer Protection
Italian Ministry of Health (Ministero della Salute)



DIABETES SURGERY SUMMIT

Clinical and Research Guidelines Development

The Diabetes Surgery Summit is endorsed by





AIMS

- To review human data describing the impact on diabetes of established bariatric operations and newer experimental procedures and devices.
- To discuss plausible mechanisms by which gastrointestinal operations might resolve diabetes, independent of their effects on body weight.
- To identify indications and contraindications for the current use of gastrointestinal surgery to treat type 2 diabetes in obese and non-obese persons.
- To develop guidelines for controlled clinical trials of diabetes surgery.

The final goal of this 2½-day meeting is to develop guidelines for the use of surgery to treat type 2 diabetes and to craft an agenda for further research.

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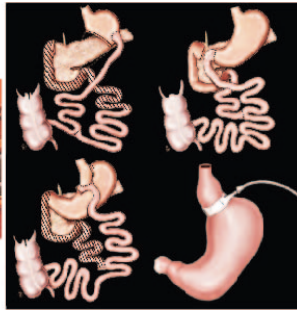
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DIABETES SURGERY SUMMIT: TOPICS

Global Burden of Type 2 Diabetes

- Epidemiology and Economics of Diabetes
- Diabetes in Developing Countries
- Complications of Diabetes: The Impact on Public Health
- Current Treatment Options: Efficacy, Costs and Complications
- Future Scenarios: The Potential Impact of Diabetes Surgery in Developed and Developing Countries

Bariatric Surgery and Type 2 Diabetes in Patients with BMI > 35 kg/m²

- Gastric Banding, VBG, RYGB, BPD: Effects on the Metabolic Syndrome
- Glucose Tolerance and Insulin Resistance
- Durability of Diabetes Control
- Morbidity and Mortality of Bariatric Surgery
- Costs of Bariatric Surgery

GI Surgery and Type 2 Diabetes in Patients with BMI < 35 kg/m²

- Diabetes Outcomes
- The Effect on Body Weight and Nutritional Status
- Glucose Tolerance and Insulin Resistance
- Morbidity and Mortality

Novel Surgical Procedures and Devices: Clinical and Animal Data

- Duodenal-Jejunal Bypass (DJB)
- Ileal Transposition (IT)
- Sleeve Gastrectomy + Enterectomy
- Omentectomy
- Intraluminal Duodenal Sleeve

Performing Future Clinical Trials of Diabetes Surgery

- What Type of Trials for What Type of Patients?
- Defining Adequate Endpoints
- Ethics of Clinical Trials in Diabetes Surgery

Mechanisms of Surgical Control of Diabetes

- Caloric Intake/Weight Loss
- Gut Hormones
- The role of incretins
- The role of the foregut
- The role of the hindgut
- Animal and Surgical Models
- Potential New Targets for Pharmacologic Research

Clinical and Research Guidelines Development



DIABETES SURGERY SUMMIT

Francesco Rubino, MD
Program Co-director



Diabetes affects more than 240 million people worldwide, and that number is expected to increase to over 380 million by 2025. Type 2 diabetes, which accounts for 90-95% of all cases, is a growing epidemic that places a severe burden on health care services, especially in developing countries.

The etiology of type 2 diabetes is still elusive, and conventional therapeutic modalities do not achieve a cure. Due to both the scale of the problem and the current epidemic growth, it is a race against time to find new approaches to better understand and treat type 2 diabetes.

Gastrointestinal surgery provides new opportunities in the fight against diabetes.

Conventional gastrointestinal operations for morbid obesity have been shown to improve type 2 diabetes dramatically, resulting in normal blood glucose and glycosylated haemoglobin levels, with discontinuation of all diabetes-related medications. Often, return to euglycemia and normal insulin levels are observed within days after surgery, suggesting that weight loss alone cannot entirely explain why surgery improves diabetes. Recent experimental studies point toward the rearrangement of gastrointestinal anatomy as a primary mediator of the surgical control of diabetes.

For these reasons, gastrointestinal surgery is a potential alternative therapy for type 2

diabetes in selected patients. Furthermore, it offers a unique opportunity to improve knowledge regarding disease pathogenesis, and it may provide insights leading to new anti-diabetes medications.

The *International Conference on Gastrointestinal Surgery to Treat Type 2 Diabetes* was developed to raise awareness of the potential for *diabetes surgery* and to set safe standards for its clinical practice. This *Diabetes Surgery Summit* will also review available data and scientific theories regarding the mechanisms of diabetes control, in an attempt to identify new avenues for diabetes research.

Following a series of presentations and discussions by prominent authorities in the field, the voting members of this conference, who represent a diversity of non-surgical and surgical disciplines, major scientific societies, and leading journals, will vote on a set of recommendations designed to capture the consensus of the group. The conference is open to a limited audience of non-voting participants who wish to observe the proceedings.

On behalf of the organizers, David Cummings, Lee Kaplan, Phil Schauer, Marco Castagneto, and myself, I would like to invite you to attend the DSS meeting in Rome. We hope that you can share our commitment for a scientific, safe, and orderly development of diabetes surgery.



DIABETES SURGERY SUMMIT TIMETABLE

Thursday, March 29th

8.30 - 18.00

8.30 - 9.10	Welcome, Introduction, Methods
9.10 - 9.40	Global Burden of Type 2 Diabetes and Markers of Cardiovascular Risk
9.40 - 10.45	Bariatric Surgery and Type 2 Diabetes in Patients with BMI > 35 kg/m ²
10.45 - 11.15	<i>Coffee break</i>
11.15 - 13.00	Bariatric Surgery and Type 2 Diabetes in Patients with BMI > 35 kg/m ²
13.00 - 14.00	<i>Lunch</i>
14.00 - 15.10	Bariatric Surgery and Type 2 Diabetes in Patients with BMI > 35 kg/m ²
15.10 - 18.00	Gastrointestinal Surgery and Type 2 Diabetes in Patients with BMI < 35 kg/m ²

Friday, March 30th

8.30 - 17.00

8.30 - 10.15	Mechanisms of Diabetes Resolution Following Gastrointestinal Surgery
10.15 - 10.45	<i>Coffee Break</i>
10.45 - 12.00	Mechanisms of Diabetes Resolution Following Gastrointestinal Surgery
12.00 - 12.45	Novel Surgical Procedures and Devices
12.45 - 13.45	<i>Lunch</i>
13.45 - 14.35	Novel Surgical Procedures and Devices
14.35 - 15.35	Current and future clinical trials
15.35 - 17.00	Diabetes Surgery: Clinical and Research Implications

Saturday, March 31st

9.00 - 15.00

9.00 - 15.00	Clinical and Research Guidelines Development
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11.35 - 11.50 Meta-analysis: Effects of bariatric operations on T2DM
Henry Buchwald

11.50 - 12.05 Specific complications of RYGB and BPD
Michel Gagner

12.05 - 12.15 Hyperinsulinemic hypoglycemia after RYGB
Allison Goldfine

12.15 - 12.30 Mortality of bariatric operations: Meta-analysis
Henry Buchwald

12.30 - 12.40 Quality insurance and hospital/surgeon qualification in bariatric surgery
Bruce Wolfe

12.40 - 13.00 Invited Critique
Allison Goldfine, Harvey Sugerman

13.00 - 14.00 Lunch

Risk/Benefit Analysis

14.00 - 14.15 Cost-effectiveness of medical treatment for type 2 diabetes
William Herman

14.15 - 14.25 Cost-effectiveness of surgical treatment for type 2 diabetes
David Flum

14.25 - 14.40 Long-term mortality risk reduction after bariatric operations
Ted Adams

14.40 - 15.10 Panel Discussion
Ele Ferrannini, David Flum, Jacques Himpens, Harold Lebovitz, Christopher Saudek, Tessa Van der Merwe

15.10 - 18.00 **Gastrointestinal Surgery and Type 2 Diabetes in Patients with BMI < 35 kg/m²** Chair: **Francesco Rubino**

15.10 - 15.20 Bariatric surgery or “Diabetes Surgery”?
Francesco Rubino

Diabetes Outcomes: Efficacy and Durability

15.20 - 15.35 LAGB vs. conventional medical treatment: a RCT
John Dixon

15.35 - 16.00 Effect of RYGB on T2DM in patients with BMI 30-35 kg/m²
Ricardo Cohen, Camillo Boza, Aureo De Paula

16.00 - 16.25 Effect of BPD on T2DM in patients with BMI < 35 kg/m²

Prospective clinical study - **Geltrude Mingrone**
Efficacy and long-term results - **Nicola Scopinaro**
BPD in patients with BMI < 30 - **Marco Castagneto**



DIABETES SURGERY SUMMIT

Clinical and Research Guidelines Development

11.30 - 12.00 Panel Discussion
Guenther Boden, David D'Alessio, Ele Ferrannini, David Kelley, Denis Richard, Luc Tappy

12.00 - 14.35 Novel Surgical Procedures and Devices

Chair: Lee Kaplan

12.00 - 12.15 Omentectomy and glucose homeostasis
William Richards

12.15 - 12.25 Sleeve gastrectomy and diabetes
Michel Gagner

12.25 - 12.45 Ileal interposition and novel combination procedures
Aureo De Paula

12.45 - 13.45 Lunch

13.45 - 13.55 Sleeve gastrectomy with mid-jejunal resection
David Cummings

13.55 - 14.15 Intraluminal duodenal sleeve and sleeve gastrectomy:
lessons from rodent models
Lee Kaplan

14.15 - 14.35 Panel Discussion
David Cummings, Aureo DePaula, Michel Gagner, Giovanni Ghirlanda, Antonio Lacy, William Richards

14.35 - 17.00 Current and Future Clinical Trials

Chair: Lee Kaplan

14.35 - 15.35 Panel Discussion
John Dixon, Ele Ferrannini, Van Hubbard, David Kelley, Carolyn Miles, Jerry Palmer, Donna Ryan, Phil Schauer

15.35 - 17.00 Diabetes Surgery: Clinical and Research Implications

15.35 - 17.00 Panel Discussion and Electronic Survey
David Cummings, David D'Alessio, Stephanie Amiel, Samuel Klein, Walter Pories, Eric Ravussin, Myrlene Staten

Saturday, March 31, 2007

9.00 - 15.00 Clinical and Research Guidelines Development

Chairs: Francesco Rubino, David Cummings, Philip Schauer, Lee Kaplan

Discussion and Voting
Diabetes Surgery Summit Faculty

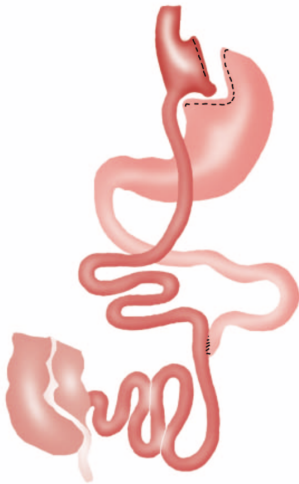
CONVENTIONAL BARIATRIC OPERATIONS

Laparoscopic Adjustable Gastric Band (LAGB)



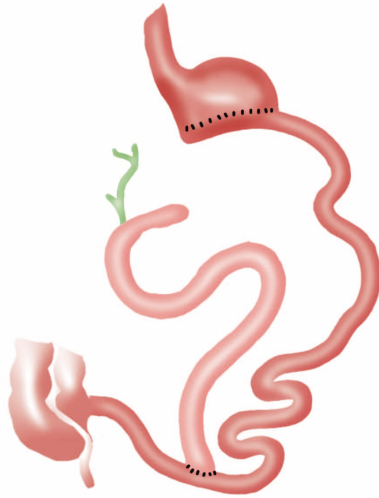
The original open gastric banding procedure, developed in the early 1990s was modified to become a laparoscopically implanted device by the mid 1990s. The LASGB is a restrictive procedure that involves encircling the upper part of the stomach with a band-like, saline-filled tube. The band is wrapped around the superior portion of the stomach, just distal to the gastroesophageal junction. The amount of restriction may be adjusted by injecting or withdrawing saline solution from the hollow core of the band through a subcutaneous port similar to that used for long-term venous access in chemotherapy patients.

Roux-en-Y Gastric Bypass (RYGB)



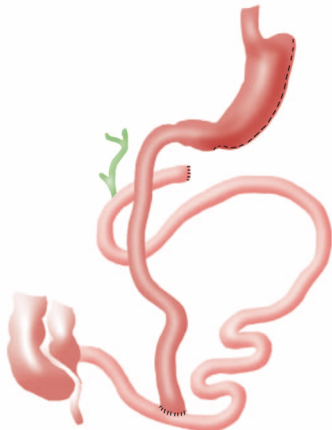
After its first report by Edward Mason (USA) in 1967, the technique of gastric bypass has undergone several modifications. The most current techniques involve the use of a surgical stapler to create a small and vertically oriented gastric pouch. The pouch is based on the lesser gastric curvature and its volume is usually less than 30 cc. The upper pouch is completely divided by the gastric remnant and is anastomosed to the jejunum (between 30 and 75 cm from the ligament of Treitz), through a narrow gastrojejunal anastomosis in a Roux-en-Y fashion. Bowel continuity is restored by an entero-entero anastomosis, between the excluded biliary limb and the alimentary limb. This anastomosis is usually performed 75-to 100 cm distal to the gastrojejunostomy (although it has been also performed at 100-250 cm in patients with BMI greater than 50 kg/m²). After RYGB, ingested food bypasses approximately 95% of the stomach, the entire duodenum and a portion of the jejunum.

CONVENTIONAL BARIATRIC OPERATIONS



Biliopancreatic Diversion- (BPD)- Scopinaro's Procedure

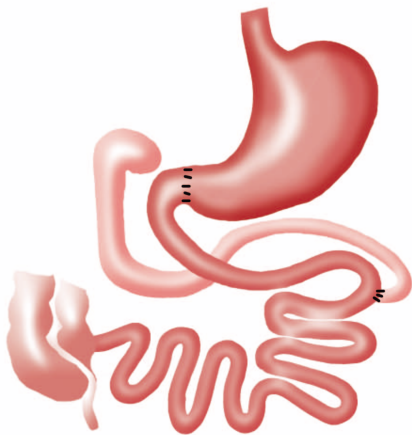
The concept of BPD was first described by Nicola Scopinaro of Genoa, Italy in 1979. Technically, the operation consists of a distal, horizontal gastrectomy which leaves behind a 200-500 ml sized upper stomach (according to individual patient's characteristics). This remnant stomach is anastomosed to the distal 250 cm of small intestine (alimentary limb). The excluded small intestine (including the duodenum, the jejunum and part of the proximal ileum) carries the bile and pancreatic secretions (biliary limb), and is connected to the alimentary channel 50 cm proximal to the ileocecal valve. This "common limb", is the only segment where bile and nutrients mix. Fat and starches are absorbed in the short common limb, whereas the alimentary limb (usually 200-250 in length) allows absorption of the non-caloric nutrients.



Biliopancreatic Diversion with Duodenal Switch- (BPD-DS)

In the BPD-DS includes a "sleeve" vertical gastrectomy (rather than horizontal as in the original Scopinaro procedure), which leaves a maximum gastric reservoir of 150-200 ml. The duodenum is closed about 2-cm distal to the pylorus and a duodeno-ileal anastomosis is performed (duodenal switch). Hence, the gastric fundus is almost entirely resected, while the antrum, the pylorus and a short segment of duodenum are preserved along with vagal nerve integrity. Bowel continuity is restored as in BPD, however, the anastomosis is performed more proximally on the alimentary limb, leaving a longer common channel of about 100 cm as opposed to the 50 cm of the original Scopinaro's procedure. The operation was conceived by Douglas Hess (Ohio, USA) but it was first published by Picard Marceau (Quebec, Canada) in 1993.

NOVEL SURGICAL PROCEDURES



Duodenal-jejunal Bypass (DJB)

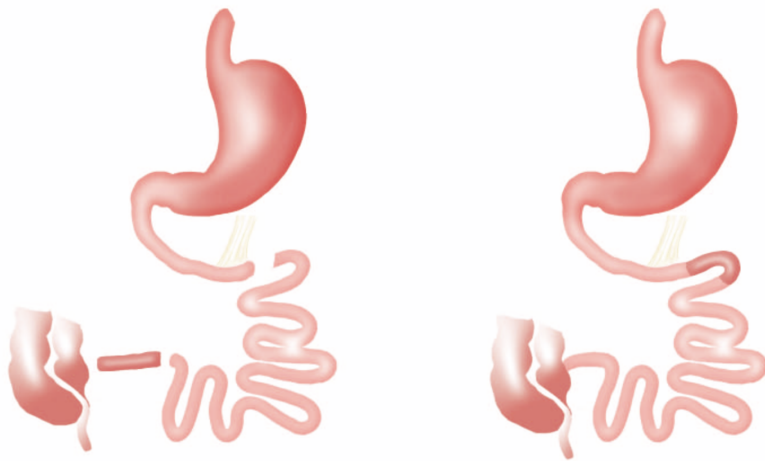
The concept of DJB was described by Dr Francesco Rubino (Italy) as an experimental anti-diabetic procedure. The operation consists of a stomach-sparing bypass of a short segment of proximal small intestine, equivalent to the amount of intestine bypassed in a standard RYGB. The duodenum and the proximal segment of jejunum are excluded from the transit of nutrients. This procedure has been shown to improve type 2 diabetes in both, lean and obese rodents (GK-and Zucker ZDF-rats). Recently, several independent investigators have performed DJB in moderately obese and overweight humans (BMI<35) showing improvement/remission of type 2 diabetes. Long-term follow up data, however, are not yet available. Two variants of DJB have been performed: one includes preservation of the pylorus and a duodeno-jejunal anastomosis; alternatively, a pre-pyloric gastro-jejunosomy can be performed.



Sleeve Gastrectomy (SG)

To shorten the duration of the laparoscopic BPD-DS in high risk patients, Dr Michel Gagner (Canada) proposed a two-stage procedure, with sleeve gastrectomy first, followed by the duodenoileostomy and ileo-ileostomy few months after. This modality resulted in drastic reduction of morbidity and mortality compared to the traditional one-stage approach in super-superobese patients (BMI > 60). Due to the remarkable weight loss induced by simply performing the sleeve gastrectomy, this procedure has been proposed as an independent anti-obesity operation by some authors. The efficacy in the long-term, however, needs to be investigated. In addition to reducing the capacity of the stomach, the procedure eliminates the ghrelin-rich gastric fundus, which may play a role in the mechanism of action of this operation.

NOVEL SURGICAL PROCEDURES



Ileal Interposition (IT)

The concept of ileal interposition, (often referred to as *ileal transposition*, although this is technically inaccurate), was first described by Koopmans and Sclafani in rodent experiments. A small segment of ileum, with its vascular and nervous supplies intact, is surgically interposed into the proximal small intestine, where its exposure to ingested nutrients is greatly increased. Animals with IT show exaggerated GLP-1 and PYY responses to nutrient loads. These hormonal changes are associated with reductions in food intake, body weight and improved glucose homeostasis, without restriction and malabsorption. Recently, an early experience with IT in lean diabetic humans has been reported (Dr De Paula, Brazil), showing improvement of diabetes in the short-term. Long-term data, however, are not yet available.



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