

27 Metabolic Syndrome— Surgical Management

Abstract: The prevalence of obesity is increasing in epidemic proportions worldwide, as is the risk for both Type 2 diabetes and heart disease. The multiple diseases or comorbidities associated with central obesity are termed the “metabolic Syndrome”, “Syndrome X,” or the “insulin Resistance Metabolic Syndrome of Obesity.” Despite aggressive management, current therapies fail to achieve satisfactory control of the problem in majority of patients. It has been observed that operations for morbid obesity not only induce weight loss but also have a significant impact on the course of the Metabolic Syndrome (MS). These procedures include Gastric Banding, Roux-en-Y Gastric Bypass and Biliopancreatic diversion. Gastric Bypass, the “gold standard procedure” for morbid obesity, has been found to have maximum impact in terms of improvement in glycemic control and overall mortality reduction.

The exact mechanism for the dramatic effect of Gastric Bypass on MS remains unknown. Various hypothesis have been proposed. Improvement in glycemic control occurs within days after surgery, long before there is any significant weight loss, and this suggests that the control of diabetes is probably mediated by changes in hormones secretion from the gastrointestinal tract. Controlled trials in centers with a wide experience of Bariatric surgery are needed to verify the possibility of a surgical cure specific to the problem. Nevertheless, early studies have shown promising results.

Mention must also be made of an experimental novel electrical stimulation device, the IGS (Implantable Gastric Stimulation) system, which can potentially improve glucose levels and induce weight loss in obese patients with Type 2 Diabetes on oral hypoglycemic therapy. Trials are underway to prove its efficacy.

INTRODUCTION

The prevalence of obesity is increasing in epidemic proportions worldwide, and subsequently raises the risk for both type 2 diabetes and heart disease.

Incidence of T2DM is increasing in Asia. India by 2025 is predicted to become the global capital for diabetes. This can be related to the growing affluence and rising incidence of overweight and obesity. International diabetes federation estimates that the number of diabetic patients in India to increase to 69.9 million by 2025. Obesity is a recognized cause of insulin resistance (IR) that leads to impaired glucose tolerance. The multiple diseases or comorbidities associated with central obesity are termed the “Metabolic Syndrome,” “Syndrome X,” or the “IR Metabolic Syndrome of Obesity.”¹ Despite aggressive management, current therapies fail to achieve satisfactory control in majority of patients.

It has been seen that operations for morbid obesity not only induce significant weight loss but also have a significant impact on the course of the metabolic syndrome (MS).

METABOLIC SYNDROME (MS)

It is a term used to define a patient who presents with 3 or more of the risk factors, listed in the Table 1.

METABOLIC SYNDROME— IS THERE A CURE?

Despite the current modalities of treatment including diet, exercise and pharmacotherapy, metabolic syndrome remains a clinical dilemma with relentless progression and far-reaching implications, there being no definitive therapy.

BARIATRIC SURGERY—A RAY OF HOPE

- Bariatric surgery could be the answer to this intriguing problem. The exact mechanism for the dramatic effect of surgical procedures for obesity on MS remains unknown.^{2,4} Various hypothesis have been proposed. Nevertheless, early studies have shown promising results. It has been documented that:
 - Bariatric surgery improves insulin Sensitivity
 - Resolution of diabetes occurs even before weight loss occurs
 - Weight loss and intake reduction do not appear the key mechanism.²

Rates of Remission in Type 2 DM (Fig. 1)

- a. Adjustable Gastric Banding -48% (slow)
- b. Roux en Y Gastric Bypass -84% (immediate)
- c. Bilio-Pancreatic Diversion -95% (immediate)

HOW DOES BARIATRIC SURGERY EFFECT TYPE 2 DM? (FIG. 2)

On the basis of their impact on Type II DM, Bariatric procedures can be categorized as following:

- Effect due to caloric restriction—Gastric banding
- Effect due to bypass of foregut and early delivery of nutrients to distal bowel—Gastric Bypass³
- Novel Procedures—effect via gastric electrical stimulation, i.e. Implantable Gastric Stimulation System

The effectiveness of gastric bypass in inducing remarkable weight loss and control of diabetes represents an “experimental model” for scientific investigations on the effects and regulation of several gastrointestinal hormones as well as an opportunity to possibly identify the pathogenetic mechanisms underlying obesity and type 2 diabetes mellitus.⁶

Proposed Hypothesis for mechanism of Action of Gastric Bypass (Fig. 3)

Several studies have investigated the hormonal changes that follow morbid obesity surgery. RYGB normalizes hyperglycemia, restores insulin sensitivity, prevents progression from impaired glucose tolerance to diabetes, and possibly reduces mortality from diabetes mellitus. Improvement in glycaemic control occurs within days after surgery, long before there is any significant weight loss, and this suggests that the control of diabetes is probably mediated by changes in hormones secretion from the gastrointestinal tract.

Gastric Bypass improves glucose homeostasis by:⁷⁻⁹

Reducing plasma levels of:

- Ghrelin⁹
- Leptin
- GIP (Glucagon dependant insulinotropic polypeptide)

Increasing plasma levels of:

- GLP-1
- PYY

Reduction of :

- GIP resistance
- Leptin resistance

RESULTS (FIG. 4)

It would be very premature to say before long- term results are available but preliminary data have been encouraging.^{10, 13} Bariatric surgery has shown to bring about significant reduction in diabetic medication usage and mortality reduction in patients of Type 2 DM.

Pre- and Postoperative usage of Anti-Diabetic Medication

In retrospective series, improvement in glycaemic control in obese patients with T2DM follows weight loss after bariatric surgery.²

Effect on Long-term Mortality Compared to Non-operated Controls¹³

| Study | Procedure | F/U | Mortality reduction |
|------------------|-----------|-----------|---------------------|
| Mac Donald, 1997 | RYGB | 9 years | 88% |
| Flum, 2004 | RYGB | 4.4 years | 33% |
| Christou, 2004 | RYGB | 5 years | 89% |
| Sowemimo, 2007 | RYGB | 4.4 years | 50% |
| O'Brien, 2006 | LAGB | 12 years | 73% |
| Adams, 2007 | RYGB | 8.4 years | 40% |
| Sjostrom, 2007 | VBG/other | 14 years | 31% |

IMPLANTABLE GASTRIC STIMULATION (IGS) SYSTEM FOR TREATMENT OF TYPE 2 DIABETES

Mention must also be made of a novel gastric electrical stimulation device which can potentially improve glucose levels and induce weight loss in obese patients with Type 2 Diabetes on oral hypoglycemic therapy. The implantable gastric pacemaker system delivers gastric contractility modulation (GCM) signals in synchrony with gastric slow waves resulting in augmentation of gastric contraction during food intake as well as amelioration of the meal induced reduction in plasma ghrelin levels.

System Components

(Tantalus Implantable Pulse Generator, Metacure, United States)

- An implantable pulse generator (IPG) that delivers non-excitatory electrical stimulation to the gastric muscle upon detection of food intake.
- An external programmer used by the physician to program and interrogate the implantable device via non-invasive telemetry.
- The TIZERTMSA and the Ultra Flex leads, proprietary bipolar, chronically implantable stitch leads.
- A portable charger, used by the patient to wirelessly charge the implantable device.
- A Patient Wand, a handheld programming device that can be used to activate the IPG.

Potential Mechanisms of Action

- Modulates satiety
- Alters hormone levels (i.e. Ghrelin, Obestatin)
- Regulates food entry into the intestine

- Modifies gastrointestinal hormones secretion
- Influences adjacent tissues via neural pathways (liver, pancreas or other GI organs).

The Procedure

The system consists of three sets of bipolar stitch electrodes that are placed in the subserosa of the gastric wall laparoscopically. One lead is placed in the fundus to detect food intake and two leads are placed in the antrum for slow wave rate detection and signal delivery (Fig. 5). Once the leads are positioned, the impedance between each bipolar electrode is assessed with an external device to ensure position. Endoscopic assessment of lead placement to rule out perforation of gastric wall, is performed during the procedure. Leads are connected to an IPG placed in a subcutaneous pocket on the left side of the abdomen.

The implantation of the system appears to be a safe procedure well tolerated by the subjects.¹⁴ Trials are underway to prove its efficacy and may eventually provide an insight into the future trends towards diabetes management.

CONCLUSION

The evidence of this extraordinary control of Metabolic Syndrome by obesity surgery stimulates another intriguing question: since surgery seems to achieve control of the disease by a primary, specific, and independent effect rather than secondary to the treatment of overweight, would it also be effective in moderately obese subjects with Metabolic Syndrome? Controlled trials in centers with a wide experience of Bariatric surgery are needed to verify the possibility of a surgical cure specific to the problem; however, surgeries for obesity seem to have a potential for changing the current concepts of the pathophysiology of the Metabolic Syndrome and, possibly, the management of this disease.

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MULTIPLE CHOICE QUESTIONS

1. **Current therapies for metabolic syndrome:**
 - A. Are 100% effective
 - B. Can prevent the development and progression of complications
 - C. Have minimal impact on the course of disease
 - D. None of the above
 2. **Gastric bypass- all are true *except*:**
 - A. Improves quality of life in obese diabetics
 - B. Reduces overall mortality rate
 - C. Produces weight loss but has no impact on insulin resistance
 - D. Improves insulin resistance
 3. **Gastric bypass - all are true *except*:**
 - A. Reduces plasma Ghrelin
 - B. Improves Leptin sensitivity
 - C. Decreases GLP-1
 - D. Increases GLP-1
 4. **Metabolic Syndrome includes all *except*:**
 - A. Central obesity
 - B. Hyperlipidemia
 - C. Hypoglycemia
 - D. Hyperinsulinemia
 5. **Regarding improvement in Type II Diabetes Mellitus:**
 - A. Gastric bypass is more effective than gastric banding
 - B. Gastric banding has no impact
 - C. Gastric banding is most effective
 - D. BPD has no impact
 6. **Implantable Gastric Stimulation (IGS) system, all are true *except*:**
 - A. Alters Gut hormone levels and modulates satiety
 - B. Has potential to induce weight loss and improve glycemic control
 - C. Electrodes are placed subserosally in the gastric antrum and fundus
 - D. Electrodes are placed in the lumen of the stomach
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1. C 2. C 3. C 4. C 5. A 6. D