

Obesity Therapy and Outcomes

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Good morning. My name is Sandeep Gupta. I am a pediatric gastroenterologist from Indiana University in Indianapolis. I have selected 20 abstracts that deal with obesity therapy outcomes. We will discuss the first 10 abstracts this morning; the next ten abstracts are worthy of reading, too. The selected abstracts cover a broad range of topics including various obesity therapies - medications, exercise, stimulation, balloon, laparoscopic surgery, Botox- complications of therapies such as strictures, and outcomes such as improvement in quality of life.

Abstract 215061: "Sibutramine significantly delays gastric emptying without altering volume or postprandial symptoms in obesity"

As you know, sibutramine inhibits reuptake of norepinephrine and serotonin; serotonin receptors are present in the enteric nervous system. The mechanisms by which sibutramine induces weight loss are unclear; specifically, whether these involve altered gastric motor and sensory function. This was a randomized, double-blind controlled study of 20 obese (BMI \geq 30 kg/m²) patients given sibutramine 15 mg a day or placebo for 12 weeks. Gastric volume and emptying were measured by scintigraphy at baseline and at 12 weeks. They measured gastric volume by SPECT and did a satiation test in which they measured maximum tolerated volume at 30 minutes and after challenge with a meal. All patients received behavioral modification classes. One subject withdrew due to hypertension (a side effect of sibutramine). There is a table at the bottom of the abstract which gives the various parameters examined – age, lean mass and gastric volume. The main result was that sibutramine delayed gastric emptying and caused weight loss. Their conclusion was that delayed gastric emptying may contribute to weight reduction seen with sibutramine.

There are many factors involved in weight loss – gastric volume, gastric tone, enteric nervous system stimulation, vagal stimulation, hormonal effects, etc. It is difficult to say what exactly caused the weight reduction with sibutramine in this study. According to this study, sibutramine delays gastric emptying which can promote satiety by stimulation of the vagus nerve by gastric distension. Could there be other reasons? Obviously that is up for debate.

The other issue is how to check for gastric volume. Ideally, one should do a three dimensional test to examine gastric volume and SPECT may not be the ideal method to study gastric volume. In this study, they did find delayed gastric emptying but not a change in gastric volume.

What is the experience with this drug in adolescents/children? Sibutramine is approved for ages 16 and older. It does seem to work in published studies (many are for 6 months), but patients also need to undergo behavioral modifications and lifestyle changes. Many adolescents however think, “As soon as I am 18, I can go get the bypass surgery done and I’ll be perfect.” They look at things in a different spectrum.

Abstract 225273: “Short duration vs. continuous bouts of exercise in childhood obesity treatment programs”

This pediatric study is from Vanderbilt University. The aim was to examine differences in compliance with exercise regimens in children. The question was how the children do with activity in short bursts of 10 minutes three times a day, or for 30 minutes once a day. This is part of an obesity lifestyle management program at the University, called Shape Down. They had the children wear RT3-triaxial accelerometer which basically monitors their activity for 11 weeks during awake hours. They served as their own control. They did one week of measurement before any intervention and then put the patients into one of two groups. Group 1 did 10 minutes of exercise three times a day. Group 2 did 30 minutes of exercise once every day. They did this for four weeks, then had a wash out period of one week where they returned to baseline. For the next four weeks, they switched groups, then had one week of wash out again. So they did four weeks of therapy, one week of wash out, four weeks of therapy, and one week of washout. They had 18 patients, ages 9 to 11. BMI was between 85th – 98th percentile which is not huge compared to adult literature. In pediatrics when we look at BMI, we don’t look at the raw number, we look at the percentile. BMI between 85th – 95th percentile is at risk for obesity which in adults translates to BMI 25-30. BMI over the 95th percentile in children is obesity. We don’t as yet have obesity 1, obesity 2, extreme obesity, super obesity or mega obesity in pediatrics. The study subjects were not very obese children who aren’t active and can’t move. They looked at self-reported compliance and compliance using the device. They found self-reported compliance to be greater for the 30 minute group than patients in the 10 minute group. When they looked at the measurement on the device, however, there was no difference between these two groups. There is subjectivity about self-reported symptoms – adherence to diet or prescription – and kids are no different than adults, I guess. Again, those that were supposed to be on a regimen of 30 minutes a day reported that they did so, but when you look at the data, they didn’t really do it any more than kids who were in the 10 minutes three times a day group.

Their conclusion was that short bursts of prescribed, physical activity did not lead to overall greater physical activity compared to a single, daily bout of exercise. We know it is very easy to preach, but when patients go home it can be difficult to practice what we tell them to do. The good news is that, unlike adults, children are intrinsically active.

Abstract 222594: “Botulinum A toxin injected into the gastric wall for the treatment of class III obesity: A pilot study”

This study is from Brazil. The authors identify obesity to be a major problem in South America. Initial studies suggest that Botox can inhibit propulsive contraction of the antral pump with a resultant delay in gastric emptying, early satiety, and weight loss. The aim of the study was to look at the effects of Botox on these parameters in obese patients. They took 12 obese patients divided into four groups. Group I got 200 units of Botox over eight sites, Group II got 2000 units of Botox (ten times more) over 16 sites, Group III got 300 units over 16 sites, and Group IV got 3000 units over 24 sites. This is a variety of therapy which makes comparison between groups quite difficult. You have a ten-fold difference in injection volume, and also variable number of sites. If I was doing this study, I probably would only change one variable. They measured gastric emptying before Botox treatment and after Botox treatment for solids and semi-solids using a ¹³C-octanoic acid and ¹³C-acetic acid breath tests, but did not do scintigraphy. Botox did not affect gastric emptying at any dose. They did not find any adverse events with Botox. On a self-reported questionnaire all patients said they had improved satiety after a meal but there was no change in gastric emptying by the ¹³C labeled breath test. They concluded that further study is needed into the use of Botox. Unfortunately, the study had no control group.

Abstract 205776: “The TANTALUS™ system for obesity: Effect on gastric emptying of solids”

This paper is from Cedars Sinai in Los Angeles. The authors looked at a new gastric electrical stimulation system, the TANTALUS system. Gastric electric stimulation has been investigated in obesity based on work of an Italian physician in the 1990s who showed that gastric stimulation helped patients lose weight. Some people are using this as a bridge to prepare patients for a surgical procedure. The TANTALUS system delivers gastric contractility modulation signals in synchrony with gastric slow waves. Their hypothesis was that by modulating the gastric contractile activity, they might affect gastric emptying and plasma ghrelin levels. They took 12 obese patients and implanted them with two pairs of gastric electrodes – four total. They don't really say where the electrodes were implanted but I would think two higher in the fundus area and two lower. They also don't say what their signal strength was – how high or low the output was. They basically did gastric emptying for solids before and after stimulation with a test meal. They gave the patient a test meal, did gastric emptying and then the stimulation some time later, I presume. The design was not very clear from the abstract. They also checked ghrelin levels at baseline and at 15, 30, 60 and 120 minutes after the meal. There were 11 females and one male with a mean age of 39 years and BMI 41 ± 3 . By stimulating the stomach, they significantly accelerated gastric emptying. The two hour retention decreased and gastric emptying accelerated with stimulation. The retention of food went down from 31% to 18%. However, there was no change in the plasma ghrelin levels with stimulation, and meals did not decrease the ghrelin levels in obese patients. They concluded that gastric modulation accelerates gastric emptying of solids but does not affect ghrelin levels. Meals did not decrease ghrelin levels in obese patients.

The study raises several issues and questions. As mentioned earlier, the design was unclear especially in regards to how ghrelin was done with respect to meals and stimulation. It was unclear if ghrelin and gastric emptying were done on separate days or on the same days. I don't think that has much bearing on the result, but I think it could have been clearer in their methods section. It was a female predominant study – 11 females, one male - and you wonder about gender differences with the system. As I understand, this is a newer system. There was some information presented yesterday about placing electrodes endoscopically on the mucosal surface. There was no data presented on it, but as a concept, should we do mucosal placement or serosal placement? It is generally done laparoscopically and takes about an hour or so to do. The other issue is that the battery dies very rapidly on these systems and better hardware would be advantageous.

Abstract 226277: “Long term follow-up of morbidly obese patients undergoing bioenterics intragastric balloon (BIB) placement”

This looks at yet another therapy. So far we have talked about sibutramine, exercise, stimulation, and Botox. This abstract looks at balloon placement. This is a bioenteric intragastric balloon (BIB). The BIB is a small balloon made out of silicone which is filled with sterile saline and inserted into the gastric lumen. It is like an artificial bezoar, like a football sitting in the stomach. Some of the issues with the earlier designs have been the balloon rubbing the side of the stomach causing gastric ulcerations and gastric mucosal damage. It appears the newer designs don't have as much of a problem with mucosal damage, as these generally tend to sit in the fundus of the stomach rather than in the antrum or distal body. The aim was to compare the long-term follow-up (27 month) of patients with balloon compared to controls. They had two groups of patients. Group A was diet and balloon (14 patients). Group B was diet alone (13 patients). They were similar in gender, age, and BMI. The 27-month follow up is one of the strengths of the study. Patients with the balloon complained of nausea and vomiting more frequently in the first six months of balloon placement, which is not surprising. You have something sitting in your stomach distending it and you feel like you have gas, dyspepsia, and discomfort. They also found that the balloon decreased the BMI in the first six months compared to controls. When you compared Group A and Group B, Group A decreased their weight more than Group B for the first six months. However, after six months, both groups regained the weight at a similar rate and there were no differences between the groups at 27 months.

Surprisingly, the abstract didn't comment on follow up endoscopy to look again at the incidence of ulceration or erosions, given the previous problems. The other concern I have is whether or not this balloon is anchored in some way, or is it just free to float throughout the stomach? We clearly need more data – balloons may be an important bridge to surgery.

Abstract 217442: “Laparoscopic Roux-En-Y gastric bypass is a viable option in the treatment of mega obesity (BMI > 70kg/m²)”

This is from Columbus, Ohio. This is on super obese patients (BMI >70 kg/m²) who were previously considered not to be laparoscopic bypass candidates. The aim of this study was to define bariatric surgery in the mega obese, BMI over 70 kg/m². This is not “extremely obese”, or “super obese”, but “mega obese”. This was a retrospective chart review of mega obese patients seen between January, 2003 and November, 2005 (19 patients – 13 females). The mean age was 42, BMI averaged 76.8, range 70.1-119.0. Mean weight was 217 kg, range 180-297 kg which is about 660 pounds. They had an average of five ± two comorbidities. Eighteen of the 19 patients had a laparoscopic procedure done successfully. In one patient, they had to do an open procedure. No re-operations, anastomotic leaks or mortalities occurred. Obviously, outcomes depend a lot on the experience of the surgeon. Five minor postoperative complications occurred and these were ileus, hypoglycemia or increased white cell count unrelated to infection. One patient had myoglobinuria that was transient. Four minor complications were seen. Five of the 19 (26%) developed a superficial wound infection, and two (2%) had a stricture at the anastomosis. The percentage of excess weight loss at six months was quite good at 24.8%. A good number of patients showed improved glucose control and blood pressure.

In summary, in this descriptive study they operated on mega obese adults with no major and four minor postoperative complications. They did have superficial wound infections, but the percentage does not seem to be much higher than what is generally reported. It is higher than what they have in their other obese patients in this group, but it is not a huge number. They had some strictures and a good amount of weight loss at six months.

Abstract 221531: “Impact of bariatric surgery on the gastro-esophageal reflux disease and esophageal motility in morbid obese patients”

This study is from Spain. It is a descriptive study looking at outcomes of therapy. Their introduction states that esophageal motility disorders and GERD are more prevalent in morbidly obese patients than in the general population. Their aim was to evaluate the effect of bariatric surgery on reflux and esophageal motility in obese patients. They took 82 patients with BMI over 40 who were prospectively evaluated before bariatric surgery and six months after bariatric surgery. They examined esophageal symptoms via questionnaire, evaluated for GERD before and after surgery using a pH probe, and performed esophageal manometry. The mean weight loss was 35 kg with a significant drop in BMI with surgery (BMI decreased from 53 pre-op to 37 post-op). A table in the abstract shows that GERD symptoms decreased and the pH probe improved after surgery. They also found that hypercontractility of the esophagus, nutcracker esophagus, was less common after surgery compared to before surgery. They conclude that surgery improved symptoms, pH probe, and esophageal motility of these patients. I wish they had a quality of life measure, which would strengthen the study.

Abstract 224494: “Incidence of stomal stricture and efficacy of endoscopic intervention: A tertiary center’s experience with gastric bypass surgery”

This is somewhat of a descriptive study from an experienced bariatric surgery center with excellent outcomes. Their aim was to report experience with stomal strictures and the methodology was to look at the bariatric surgery patients from January, 2000 through August, 2004. They looked at the medical records of 888 bariatric surgery patients. Ninety-four (10.6%) underwent endoscopy to check for strictures. Of those that underwent endoscopy, about half had a stomal stricture. Overall, 58 (6.5%) had a stomal stricture. That incidence, I think, is somewhat lower than other reports – at our center it is about 8-12%. They provide a ton of descriptive data in the abstract. The 58 patients with a stomal stricture underwent 125 dilations for the strictures. The postoperative days to endoscopically confirm a stricture was anywhere from 12 to 365 days. The mean time to stricture was 66 days. They used endoscopy as the gold standard for checking for strictures, compared to this radiography, had a sensitivity of 66%, a specificity of 83%, a positive predictive value of 85%. So, if you see something wrong on the x-ray, they are going to have an abnormal endoscopy. But the negative predictive value was only 57% so that a normal radiological study does not rule out a stricture.

They don’t tell us what prompted the endoscopy – were the patients symptomatic, were they being screened, were they just nauseous or were they experiencing hypoglycemia? They don’t tell us how sick these patients were. They also do not indicate the criteria for evaluating strictures. The take home message from this is that you should not depend on x-ray as the gold standard for strictures.

Abstract 223676: “Role of Peptide YY in ileal brake induced satiety and proximal gastric function”

This is from the Netherlands. This was a difficult to read abstract mainly because of the several experiments and interventions. The methodology was not completely clear, so I had to make some assumptions. Activation of the ileal brake with ileal fat perfusion induces satiety and reduces food intake. Basically, fat in the ileum will induce the ileal brake which will then cause satiety and reduce food intake. Peptide YY (PYY) is secreted from the L cell in the distal GI tract and the release has two mechanisms. In neurally mediated release, when we eat food, a nerve signal is sent to release PYY; in food mediated release, as the food enters the small bowel, it directly stimulates the L cells to release PYY. They wanted to see if PYY is a mediator for the ileal brake. They perfused the ileum with fat (intralipid), caused the ileal brake and asked, “What is the mechanism for the ileal brake? Is it PYY?” They took 16 healthy controls, 7 males and 9 females with an age range of 22-53 years. In one group, they did ileal fat

perfusion with intralipid. They don't tell how the infusion was done - was it an NG tube? How far did the tube go down? It couldn't be a tube from the rectum, so we don't know how the ileal fat infusion was done. The control group received saline. The second group received an infusion of peptide YY. I am presuming it was given intravenously - they gave a low dose and a high dose. The infusion was done over a number of hours on two separate occasions also. So, one group got ileal fat and the other group got an infusion of PYY. They did this fasting and in response to a meal. In the group that got the ileal fat, there was an increase in plasma PYY; this group also had increased satiety compared to patients who received PYY infusion. They found that the fasting and postprandial gastric volumes were higher in patients who received the ileal fat infusion than PYY. To summarize this study, the authors state that ileal fat induced satiety by increasing the gastric volume. The data would suggest that PYY does not have a role in ileal brake.

Questions raised by this study are many. How does ileal fat increase the gastric volume? Is exogenous PYY different from endogenous PYY? Is the rate of release of PYY a factor? Are there other factors? Are you getting neural stimulation at the same time? I would not take the results as proof that PYY is not involved in the ileal brake, but the study gives a different way of looking at things.

Abstract 226427: "Alterations in gut PDK4 and calpain-9 are associated with improved insulin sensitivity following Roux-en-Y gastric bypass surgery"

This relates to alteration in gut PDK4 and calpain-9 with bariatric surgery. These hormones are associated with insulin resistance/sensitivity. They took five obese females and performed gastric and jejunal biopsies before surgery and six months after surgery. They looked for expression of the hormones PDK4 and calpain-9 known as CAPN-9. They found that the BMI decreased in the patients after surgery, PDK4 decreased after surgery, CAPN-9 increased after surgery and the insulin sensitivity improved. CAPN-9 improves insulin sensitivity and that PDK4 decreases sensitivity; low PDK4 is good, high CAPN-9 is good. They found a decreased expression of PDK4 and increased expression of CAPN-9 on biopsy after surgery which improved insulin sensitivity.

Thank you so much for you time, the lively discussion and sharing your experiences.

Abstracts Discussed

215061: Sibutramine Significantly Delays Gastric Emptying without Altering Volume or Postprandial Symptoms in Obesity. *Maria I Vazquez-Roque, Debra Stephens, Duane Burton, Kari Baxter, Michael Ryks, Matthew Clark, Michael D Jensen, Sarah Kalsy, Karen Graszer, Alan R Zinsmeister, Michael Camilleri*

Background: Sibutramine is associated with weight loss and acts as a noradrenergic (NE) and serotonergic (5-HT) reuptake inhibitor. NE and 5-HT alter gastric functions. It is unclear whether weight loss with sibutramine is associated with altered motor and sensory functions of the human stomach. Aim: To compare in a randomized, double-blinded, controlled study with concealed allocation the effects of placebo and sibutramine, 15 mg daily for 12 weeks, on gastric volumes, emptying, maximum tolerated volumes (MTV) and post-challenge symptoms in obese volunteers who were otherwise healthy. Methods: We planned a study of 24 obese [body mass index (BMI) >30kg/m²] participants and documented lean mass and % fat by body composition (DEXA). All subjects underwent at baseline and post-treatment the following measurements using validated tests: gastric emptying for solids and liquids by scintigraphy (GE t1/2); gastric volumes by SPECT; maximum tolerated volume and 30 minute post-challenge symptoms by satiation test. All participants received the same behavioral modification classes using the LEARN manual. Statistical analysis used ANCOVA with baseline observations, gender, and BMI as covariates. Results: To date, 20 people have completed all studies. One subject was withdrawn due to hypertension. The table summarizes the data baseline and post-treatment, mean±SEM. Changes in weight were -0.9±1.2kg for placebo and -4.4±0.9kg for sibutramine (p=0.034). Changes in BMI were -0.1±0.4 kg/m² for placebo and 1.6±0.3 kg/m² for sibutramine (p=0.011); changes were somewhat more pronounced in females. No significant differences in lean mass or % fat were noted in the two treatment groups. There was significantly delayed gastric emptying of solids and liquids with sibutramine, but no treatment differences in gastric volumes or satiation. Conclusion: Delayed gastric emptying may contribute to the weight reduction in response to sibutramine in obese people.

	Placebo, n=10, BL	Placebo, POST	Sibutramine, n=10, BL	Sibutramine, n=10
Age, y	45±4	45±4	43±4	42±4
Lean mass x 10 ⁻³	50.9±4.6	48.8±3.3	48.7±3.6	52.1±3.1
Tissue fat, %	49.2±3.4	47.4±0.66	47.6±2.3	46.2±0.66
Fasting gastric vol, ml	215±15	243±20	257±20	232±21
Δ PP vol, ml	453±26	446±22	464±27	435±22
MTV, ml	1289±133	1242±94	1224±71	1129±94
Aggregate symptom score	158±22	178±21	122±14	174±21
GE t1/2 solids, min*	119±16	108±6	119±12	129±6
GE t1/2 liquids, min#	21±4	15±4	21±3	30±4

* p<0.05; # p<0.01

225273: Short Duration Vs Continuous Bouts of Exercise in Childhood Obesity Treatment Programs. *Sari Acra Megan Neumman, Andrea Klint, Kong Chen*

Introduction: Exercise and increased physical activity (PA) are integral to life-style weight management programs in obese children and success hinges on compliance. Studies have shown that children appear to spontaneously perform leisure PA in short bursts. We examined whether exercise regimens tailored after this pattern (10 min tid) led to increased compliance and total daily PA compared to a single bout of 30 min/day by obese children as part of a 10-week obesity lifestyle management program (ShapeDown). Both exercise prescriptions were for greater than moderate intensity PA performed daily. Methods: Using a randomized, crossover design (investigator- blinded), this pilot study examined PA patterns in 9 boys and 9 girls, ages 9-11, BMI 85-98%. Minute-by-minute PA during awake hrs was monitored using an RT3 tri-axial accelerometer continuously for 11 weeks, including 1 week prior to any intervention (baseline 1 PA). Participants then entered the program and were randomized to: (Group 1) 4 wks of 10 min .tid of exercise (period 1) followed by 4 wks of 30 min q day (period 2), or to (Group 2) 30min q day x 4 wks (period 1) followed by 4 wks of 10 min t.i.d (period 2). A 1-week washout period followed by a second 1-week baseline (baseline 2 PA), during which ad-lib PA occurred, separated each exercise period. Results: Baseline characteristics were similar between Groups 1 and 2 (BMI, gender, race, baseline 1 and 2 PA). Furthermore, Groups 1 & 2 had similar changes in BMI (p=0.98; -0.02 +/- 0.03 vs -0.02 +/- 0.04, respectively) and dietary intake by 24-hr (0.4 % vs. 1.8%, p=0.42) over the study period. While self-reported compliance was significantly greater for 30 min q day vs. 10 min t.i.d, measured compliance using accelerometers was similar between the two exercise forms (31% vs 55%, respectively; t-test, p=0.12). The normalized average changes (from the respective baselines) in PA during interventions were 1.06 +/- 0.27 for 10 min t.i.d and 1.11 +/- 0.31 for 30min q day (p=0.67). No carryover or period crossover effects were noted.

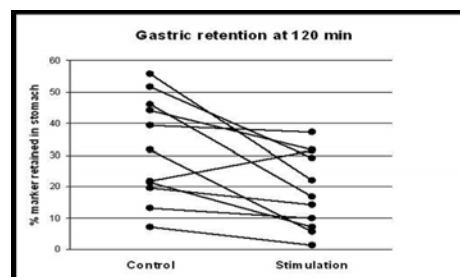
Conclusion: Short bursts of prescribed PA did not lead to an overall greater daily PA compared to a single daily bout of exercise, an effect mediated at least in part by poor compliance with both forms of exercise in obese children undergoing a life-style modification weight management program. This highlights the challenges facing obesity intervention programs in children.

222594: Botulinum A Toxin Injected into the Gastric Wall for the Treatment of Class III Obesity: A Pilot Study. *Aloisio Cardoso Jr., Paulo Roberto Savassi-Rocha, Luiz Gonzaga Vaz Coelho, Maria Matilde Mello Sposito, Walton Albuquerque, Marco Tulio Costa Diniz*

BACKGROUND - Obesity represents a main public health problem in western countries. Initial studies suggest that injection of botulinum A toxin (Btx-A) into the antropyloric region inhibits propulsive contractions of the antral pump, with delay in gastric emptying, early satiety and body weight loss. **METHODS** -After approval by University Ethics Committee, we prospectively evaluated 12 patients with class III obesity divided into four groups of three patients each. In groups I and II, 200 U Btx-A were injected into the antropyloric region at 8 and 16 sites, respectively. Groups III and IV received 300 U Btx-A into the antropyloric region at 16 and 24 sites, respectively. Body weight and gastric emptying time (GET) of solids and semi-solids using ¹³C-octanoic acid breath test and ¹³C-acetic acid breath test, respectively, were determined before and after injection over a period of 12 weeks. **RESULTS** - Pre- and post-treatment body weight or solid and semi-solid GET did not differ significantly between groups ($p>0.05$). All patients reported a feeling of early satiety. No adverse effects related to Btx-A or complications resulting from the endoscopic procedure were observed. **CONCLUSION** - The injection of different doses of Btx-A at different sites in the antropyloric region of patients with class III obesity did not interfere significantly with the solid and semi-solid GET or body weight of these individuals. However, early satiety was reported by all patients, the procedure was safe and no side effects of the treatment were observed. Further controlled studies involving different methodologies regarding dosage of Btx-A and sites of injection are necessary.

205776: The TANTALUS™ System for Obesity: Effect on Gastric Emptying of Solids. *Claudia P Sanmiguel, Scott A Cunneen, Edward H Phillips Edy E Soffer*

Background: Gastric electrical stimulation (GES) is currently investigated for the treatment of obesity. The TANTALUS System delivers gastric contractility modulation (GCM) signals in synchrony with gastric slow waves, resulting in significant augmentation of gastric contractions during food intake. We hypothesized that such modulation of contractile activity may affect gastric emptying and plasma ghrelin levels. **Aim:** To test the effect of GCM of the gastric antrum on gastric emptying of solids and ghrelin levels. **Methods:** 12 obese subjects were implanted with 2 pairs of antral electrodes and an implantable pulse generator (IPG, TANTALUS™). Gastric emptying test (GE) for solids was performed twice, on separate days, in each subject, starting few weeks after implantation: 1) control, before the start of stimulation, and 2) with stimulation, after device was turned on. Blood samples for ghrelin, were taken at baseline, and at 15, 30, 60 and 120 min after the test meal. Results as mean \pm SD, analysis by t-test and $p<0.05$. **Results:** 11 females, 1 male, age: 39.1 ± 8.9 years, BMI: 41.6 ± 3.4 , 3 subjects with type 2 diabetes. One diabetic patient did not complete GE test because of technical issues. GCM significantly accelerated gastric emptying: retention at 2 hours $18.7\pm 12.2\%$ vs. $31.9\pm 16.4\%$, stimulation vs. control respectively, $p=0.008$. T $1/2$ 78.3 ± 23.5 vs. 95 ± 31.7 min, stimulation vs. control respectively, $p=0.04$. Mean results for gastric emptying were within normal at both baseline and stimulation. Meal ingestion induced only minimal, insignificant reduction in ghrelin levels. There was no significant difference in AUC of ghrelin between control and stimulation. **Conclusions:** 1) After GCM stimulation, there is significant acceleration of gastric emptying of solids in obese patients, without affect on ghrelin levels. 2) The obese subjects did not exhibit the significant, meal-induced reduction in ghrelin.



226277: Long Term Follow-Up of Morbidly Obese Patients Undergoing Bioenterics Intra-gastric Balloon (BIB) Placement. *Spyros Michopoulos, Georgios Stamatis, Stephanos Karagiannis, Fotis Dimopoulos, Helen Chrysanthopoulou, Chris Karatsoras, Emmanouel Archavlis, Michael Theodorakis, Athanassios - Meletios Dimopoulos*

The obesity worldwide epidemic poses serious health hazards, particularly in Western societies. Current clinical evidence suggest that surgery offers significantly beneficial long term results to people with morbid obesity, compared to conventional methods, since even modest weight loss is associated with substantial reduction of co-morbidities. However, a large number of patients are unwilling to undergo surgical procedures. Alternatively, the BIB® System consists of a small size, silicone-made balloon, filled with sterile-saline water that can be inserted via endoscopy so that the stomach is partly filled. To our knowledge, reports of long term results with this procedure is scarce in the literature. The aim of our study was to follow-up and compare two groups of obese (BMI > 40 kg/m²) patients: Group A (N=14) was comprised of those reluctant to surgery, who underwent the BIB procedure, whereas patients of the other group (Group B; N=13) were only put on appropriate low caloric diet. Group A patients were put on the same diet scheme as those in Group B through out the follow-up period. Results: All patients were hospitalized for 1-4 days after the procedure. Discomfort, nausea and vomiting occurred frequently but did not lead to BIB removal during the first 6 months. There were no statistical differences in age, gender ratio, duration of follow-up period and initial BMI between groups. However, the magnitude of BMI reduction was significantly higher at 6 months as well as at the end of the follow-up period in patients having undergone the BIB procedure, compared to those that underwent no intervention. Results are summarized in the table (Mean ± SD). Conclusions: 1) The BIB® System leads to significant short- as well as long-term weight reduction in patients with morbid obesity, mainly when patients concurrently adhere to a diet protocol 2) Unfortunately, most patients regain weight in the long term although significantly less so following the BIB procedure. The persistence of difference is mainly due to the initial (during the first 6 months) weight loss, as the regain after the 6th month is the same in both groups.

	Group A	Group B	p
Age (years)	41.0 ± 7.9	40.7 ± 12.3	NS
Men/women	4/10	5/8	NS
Follow-up (months)	27.0 ± 4.9	27.2 ± 7.5	NS
BMI (at entry)	46.1 ± 4.4	46.7 ± 6.4	NS
ΔBMI (6 months)	-7.0 ± 2.8	-4.3 ± 1.88	0.008
ΔBMI (throughout follow up)	-4.6 ± 3.2	-0.96 ± 1.64	0.001
ΔBMI 6th month to the end	2.3 ± 1.4	3.0 ± 2.1	NS

217442: Laparoscopic Roux-En-Y Gastric Bypass is a Viable Option in the Treatment of Mega Obesity (BMI >70kg/m²). William Watson, Bradley Needleman, Vimal Narula, S. Scott Davis, Matthew Goldblatt, W. Scott Melvin, Dean Mikami

Purpose: Super-obese patients (body mass index (BMI) > 50 kg/m²), were previously not considered candidates for laparoscopic Roux-en-y gastric bypass (LRYGB) surgery. As surgical experience and technology improves, LRYGB in the super obese has become more widely accepted. The aim of this study is to define a new classification of obesity (megaobesity, BMI > 70 kg/m²), as well as to evaluate the outcome of LRYGB in this patient population. Methods: We conducted a retrospective review of patients with BMI > 70 kg/m² undergoing LRYGB at a single university-based comprehensive weight loss program from January 2003 - November 2005. We reviewed preoperative demographics, operative techniques and postoperative course. Results: Nineteen patients were eligible for the study (13 female, 6 male), with an average age of 42.1 ± 8.3 years of age. Preoperative mean weight was 217 kg (range: 180 - 297 kg). Preoperative mean BMI was 76.8 kg/m² (70.1 - 119.0 kg/m²). Patients were 261 ± 56% above their ideal bodyweight. Patients had on average 5.0 ± 2.5 co-morbidities attributed to obesity, and averaged 6.5 ± 3.6 medications for those co-morbidities. Eighteen of 19 cases were completed laparoscopically. One surgery was converted to open secondary to adhesions from previous surgeries. No patients required re-operation. There were no mortalities or anastomotic leaks. Operating times were 121.1 ± 43.4 minutes. Peri-anastomotic drains were placed in 9 of 19 patients (47%) and all were removed prior to discharge. There were 4 minor postoperative complications in 4 patients: ileus, hypoglycemia, asymptomatic elevated WBC without source and myoglobinuria treated with hydration and alkalinization of urine. Hospital stays was 3.3 ± 1.7 days. Percent excess weight loss (%EWL) was 14.3 ± 2.9% at 2 months (m) postoperative (n=14), 24.8 ± 4.3% at 6 m postoperative (n=8) and 42 ± 6.6% at 12 m (n=6). Five of 19 patients (26%) developed superficial wound infections. Two patients (11%) developed anastomotic strictures. Four of 9 patients (44%) reported decreased insulin requirements, 4 of 9 patients (44%) discontinued as least 1 oral hyperglycemic agent and 3 of 12 patients (25%) stopped at least one antihypertensive drug by 2 months postoperatively. Summary: LRYGB is a technically feasible surgery in the megaobese. Operative times are similar to LRYGB patients with a BMI of < 70 kg/m². Superficial wound infections appear to be more prevalent in the megaobese. Percent EWL at 6 months are similar to those with a BMI of < 70 kg/m². Long term follow-up will provide more information on resolution of comorbidities. LRYGB is a viable treatment option in the treatment of megaobesity.

221531: Impact of Bariatric Surgery on the Gastro-Esophageal Reflux Disease and Esophageal Motility In Morbid Obesity Patients. *Vicente Ortiz, Ponce Marta, Marisa Iborra, Belen Beltran, Bastida Guillermo, Jose*

Esophageal motility disorders and gastro-esophageal reflux disease (GERD) are more prevalent in patients with morbid obesity (MO) than in the general population. However, the influence that bariatric surgery have on these variables is unknown. Aim: To evaluate the influence that bariatric surgery have on GERD and esophageal motility. Methods: Eighty-two consecutive patients with MO (body mass index (BMI) \geq 40 kg/m²) were prospectively evaluated before and six months after having bariatric surgery. In all cases the surgical technique used was a vertical gastropasty plus a gastro-jejunal bypass. The parameters investigated were: 1) Esophageal symptoms registered through a structured clinical questionnaire. The consensus diagnostic criteria for GERD of having two or more episodes of heartburn in one week was used. 2) Esophageal exposure to acid which was achieved through a pH-metry (considered positive when time of exposure to pH < 4 was greater than 5 % of the time). 3) Alterations of esophageal motility observed in a manometry. None of the patients was on anti-secretory therapies at least for 10 days previous to their evaluation. Results: The mean age of the patients was of 41.3 \pm 10.1 years (61 women/21 men). The BMI previous to surgery was of 50.1 \pm 6.4. Six months after the bariatric surgery their BMI was 37.5 \pm 5.4 with a mean weight loss of 35.6 \pm 13.2 Kg. The main changes observed on symptoms and esophageal function are shown in table. The prevalence of GERD (symptoms) and the rate of pathological exposure to acid (positive pHmetry) were significantly reduced six months after the bariatric surgery. The percentage of time with pH < 4 (n=82) was 8.1 \pm 11.8 (females 5.9%/males 14.7%) and after the surgery was 2.9 \pm 5.4 (females 3.1%/males 2.6%) (p=0.005). The initial lower esophageal sphincter pressure was of 14.9 \pm 7.0 mmHg and it was not modified after surgery. The manometry of the MO patients showed that they had an hyper-contractile oesophagus (nutcracker pattern which is defined by presenting peristaltic waves with a mean amplitude > 180 mmHg) in the 18.3 % of the patients. This percentage was reduced after surgery to 6.1 % of the patients. No other changes in the esophageal motility was observed after surgery. Conclusion: The prevalence of GERD (symptoms and pHmetry) and their esophageal hypercontractility decrease after bariatric surgery in patients with MO.

n=82	Basal	After Surgery	p
Symptoms	15(18.3%)	2(2.4%)	0.001
positive pH-metry	40 (48.8%)	15(18.3%)	<0.0001
Nutcracker pattern	15(18.3%)	5(6.1%)	0.021

224494: Incidence of Stomal Stricture and Efficacy of Endoscopic Intervention: A Tertiary Center's Experience with Gastric Bypass Surgery. *Michael A Veliuona, Fedele J DePalma, Robert N Cooney, Abraham Mathew*

Introduction: The Roux-en-Y gastric bypass is a highly effective surgical approach for morbid obesity but is not without associated complications. We report our institution's experience with gastric bypass surgery and endoscopic intervention in treating stomal strictures. Methods: Patients who had undergone gastric bypass surgery at our institution between January 2000 and August 2004 were identified. Medical records were reviewed to obtain pertinent patient demographics and peri-operative data and outcomes. Results: Eight hundred and eighty eight patients underwent gastric bypass surgery at our institution by one of five surgeons. Among these patients, 94 (10.6%) underwent esophagogastroduodenoscopy (EGD) for evaluation of possible stomal stricture and 58 (6.5%) were found to have one. Laparoscopic approach was associated with more strictures (43 or 74.1%, p=0.0003). When controlled for the laparoscopic procedures, stomal stricture rate was similar between high volume and low volume surgeons. A total of 125 dilations were performed with an average of 2.2 dilations per patient (range 1-7). There was a total of 4 perforations (3.2%) related to endoscopic dilation and 3 (75%) perforations occurred in patients who had undergone repeated EGD and dilations (2, 5, 7 dilations). The one patient in which a perforation occurred with a single dilation was dilated to 20 mm. The other 3 perforations occurred with dilations to 10 mm and 12 mm (2). The average number of post-operative days for endoscopically confirmed strictures was 66.2 days (range 12-365). Of the 94 patients thought to have stomal strictures, 87 underwent either computed tomography (CT scan) or barium Xray prior to endoscopic evaluation. Abnormal radiographic findings were seen in 42 patients and 5 (11.9%) of these patients had a normal EGD without evidence of stomal stricture. 19 (42.2%) patients with normal radiologic studies were found to have stomal strictures requiring dilation. Using EGD as the gold standard, radiographic studies demonstrated a sensitivity of 66% (95% CI: 52-77), specificity of 83% (95% CI: 65-93), positive predictive value (PPV) of 88%, and negative predictive value (NPV) of 57%. Conclusion: Endoscopic dilation of stomal strictures at our institution is safe with a perforation rate at the low end of the published range. Radiographic findings can assist in diagnosing the presence or absence of stomal strictures, but there is not always a direct concordance between radiographic and endoscopic findings.

223676: Role of Peptide YY in Ileal Brake Induced Satiety and Proximal Gastric Function. *My K Vu, Jeroen W Maljaars, Izak Biemond, Banafsche Mearadji, Ad Masclee*

Activation of the ileal brake with ileal fat perfusion induces satiety and reduces food intake. Peptide YY (PYY) is considered as mediator of the ileal brake. Recent studies indicate that PYY influences satiety but the role of PYY as physiological mediator is under debate. The present study was undertaken to compare the effects of ileal brake activation with ileal fat (endogenous PYY release) versus exogenous PYY infusion on satiety and proximal gastric motor function. Two protocols were performed in 16 healthy volunteers (8 per protocol; 7M, 9F; age 22-53 yr). Study A: ileal fat perfusion (Intralipid 20%, 2 kcal/min for 3 hrs) versus saline (control) on two separate occasions. Study B: PYY 3-36 infusion at low and high doses of 15 and 30 pmol/kg/hr vs. placebo, on three separate occasions. Studies were performed in the fasting state and in response to a 200 ml, 300 Kcal liquid meal. Parameters studied were: plasma PYY (RIA), satiety (hunger, fullness, wish to eat, nausea) by visual analog scale (range 0-100mm) and proximal gastric motility (volume by barostat). Results: Ileal fat significantly ($p<0.05$) increased plasma PYY from 15 ± 1 to 26 ± 2 pM. During PYY infusion plasma levels of 28 ± 3 pM (with the dose of 15 pmol/kg/hr) and 55 ± 10 pM (with the dose of 30 pmol/kg/hr) were reached. Ileal fat significantly ($p<0.01$) increased satiety (fullness increment 15 ± 3 mm) in contrast to PYY (fullness increment 2 ± 1 mm). In the postprandial state, ileal fat also significantly ($p<0.01$) increased satiety (meal+ileal fat vs meal+placebo: fullness increment 25 ± 3 vs 12 ± 3 mm) while exogenous PYY did not further increase satiety (meal + PYY vs. meal with placebo : fullness increment 11 ± 2 vs. 10 ± 2 mm). The same was true with respect to hunger scores. Fasting gastric volume (barostat) increased significantly ($p<0.01$) in response to ileal fat (from 150 ± 14 ml to 433 ± 54 ml) but not in response to PYY 3-36 infusion (from 162 ± 18 ml to 180 ± 19 ml; n.s.). In all experiments ingestion of the meal resulted in an identical increase in proximal gastric volume to a volume of 400-450 ml at 15 min postprandially. Postprandial proximal gastric volume at 90 min after meal ingestion was significantly ($p<0.01$) higher during ileal fat vs. control (410 ± 42 ml vs 183 ± 20 ml) while PYY infusion did not affect volume over control (230 ± 19 ml vs 187 ± 15 ml). It is concluded that ileal fat induces satiety and results in proximal gastric relaxation, in contrast to exogenous PYY 3-36 at identical plasma levels. These data do not support a role for PYY as physiological mediator in ileal brake induced satiety or ileal brake induced proximal gastric relaxation.

226427: Alterations in Gut Pdk4 and Calpain-9 Are Associated with Improved Insulin Sensitivity Following Roux-En-Y Gastric Bypass Surgery. *Edward Lin, Ih-Ping Huang, Leena Khaitan, Li Gu, Thomas R Ziegler, C. Daniel Smith, Nana Gletsu*

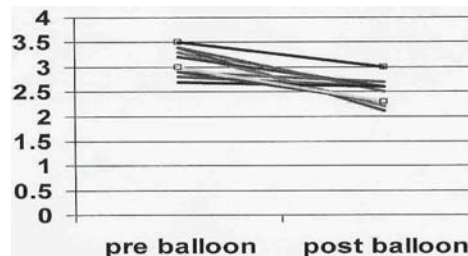
BACKGROUND: Pyruvate dehydrogenase kinase-4 (PDK4) and Calpains (CAPN) are novel hormones that affect insulin resistance. Skeletal muscle PDK4 downregulates pyruvate dehydrogenase activity which inhibits glucose utilization. CAPN have been shown to improve peripheral glucose transport by facilitating GLUT4 translocation. Insulin resistance is associated with inappropriate levels of PDK4 and CAPN, and restoration of normal expression improves insulin sensitivity. We studied the effects of roux-en-Y gastric bypass surgery (RYGB) on gut PDK4 and CAPN-9 (gut specific) expression and its association with insulin resistance. METHOD: Five severely obese women (BMI 49.7 ± 1.1) were admitted to the General Clinical Research Center for IVGTT studies at baseline and at 6 months following RYGB. Gastric and jejunal mucosa were biopsied from identical sites at baseline and at 6 months. PDK4 and CAPN-9 gene expressions were determined using microarray analysis and independently confirmed using RT-PCR. Results are reported as means \pm SEM. RESULTS: BMI at 6 months was 36.3 ± 1.6 . Overall gastric and jejunal PDK4 expression was downregulated at 6 months, while CAPN-9 was upregulated. The most significant change was seen in a reduction in gastric PDK4 (densitometry 1.0 ± 0.1 to 0.64 ± 0.06 , $p=0.01$, and an 8.7 fold decrease by microarray analysis). There was an overall 50% increase in insulin sensitivity (Si) at 6 months. CONCLUSIONS: This is the first documentation of alterations in gut PDK4 and CAPN-9 expression following RYGB, which are associated with significantly improved insulin sensitivity. These changes in hormone expression may provide an additional mechanism for the resolution of type-2 diabetes observed following RYGB.

Additional Reading: Obesity Therapy and Outcomes

222947: Gastric Electrical Activity Before and After Bionterics Intra-gastric Balloon (BIB) Placement. *Gustavo A Torres-Barrera, Francisco Bosques-Padilla, Hector Maldonado-Garza*

BACKGROUND: Obesity is increasing worldwide. BIB has been used by some groups as an alternative to Surgery or in preparation to it. The mechanisms involved are partially studied. Recently the effect of BIB has been published, observing a reduction in Ghrelin levels as a factor in BIB effect. We hypothesized that the presence of the BIB can promote gastric dysrhythmia, and early satiety. AIM: The aim of this study was to evaluate the effect of the presence of BIB on gastric electrical activity. METHODOLOGY: We included 15 overweight patients that meet the following criteria: 1) Body Mass Index (BMI) above 30, 2) Age above 18, 3) Informed consent. Exclusion criteria: 1) Previous gastric surgery, 2) Associated diseases with effect on gastric motility 3) Peptic ulcer or erosive esophagitis, 4) Hiatal hernia >3 cms. METHODS. An electrogastrogram (EGG) was performed before and one month after BIB placement. We used a Medtronic polygraph and EGG software. The procedure was performed early in the morning, after an overnight fast and in the absence of medication with effect in motility.

The recording included a preprandial and a postprandial period. We used a standard meal (250grs normal yogurt providing 204kcal) We evaluated the results in frequency in cpm in channels with the best recording of the electrical activity. A Wilcoxon test was used in statistical analysis. RESULTS. Patients were 13F/2M, mean age 34±8 range 20-51; mean BMI 36±4 range 30-43.6. In every patient gastric electrical activity before BIB placement was in the normal range (2.5-3.5cpm). Frequency was significantly reduced after BIB placement in all patients $p<0.001$ and in 6 /14 reduction was below the normal range. Conclusion. BIB reduced gastric electrical activity in obese patients which can be one of the mechanism involved in its satiety effect.



225346: CNS Expression of Ghrelin and Cholecystokinin (CCK) with Gastric Electrical Stimulation in Rats. *Suhuan Liu, Ming Tang, Shangmin Tao, Jiande Chen*

Background and aim: Gastric electrical stimulation (GES) has recently been shown to be safe and effective in the treatment of obesity, in the peripheral tissue, it induces gastric distention, impairs gastric myoelectric activity, delays gastric emptying, but its effects in the central nervous system (CNS) are remained unclear, the aim of this study was to explore the possible central mechanisms involved in GES by investigation of the expression of food intake-related peptides. Methods: the experiment was designed in two parts: an acute experiment with 2h GES and a long term experiment with 14- day continuous GES, each experiment contained two groups: stimulation group and Control group. After stimulation, the expression of orexigenic hormone - ghrelin in the hypothalamus and anorexigenic hormone -CCK in the hippocampus were detected by immunohistochemical method. GES was performed using pulse trains (train on-time of 2s, off-time of 3s, pulse amplitude of 6mA, width of 0.3ms and frequency of 40Hz). Results: Compared with the control group, 2h GES resulted in a decrease in the number of ghrelin immunoreactive neurons in the hypothalamic paraventricular nucleus (PVN, 34.8±1.86 vs. 57.2±2.95, $P=0.02$) and in the supraoptic nucleus (SON, 51.2±3.21 vs. 82.8±3.08, $P=0.01$). The number of CCK immunoreactive neurons in the hippocampus was of no changes (7.4±0.87 vs. 6.2±0.58, $P=0.29$). After 14-day GES, the number of CCK immunoreactive neurons in the hippocampus was increased compared with that of the control group (4.0±0.32 vs. 2.4±0.51, $P=0.03$). However, there were no changes of the number of ghrelin immunoreactive neurons either in the PVN (55.5±5.49 vs. 61.6±3.53, $P=0.66$) or in the SON (65.5±3.13 vs. 80.0±3.39, $P=0.20$). Conclusions: These results indicate that the expression of ghrelin and CCK can indeed be altered by GES. For the first time, we have demonstrated that GES may alter energy homeostasis by modulating the expression of food intake-related hormones in the central nervous system-reducing acutely the level of orexigenic ghrelin and increasing chronically the level of anorexigenic CCK.

217257: Post Adjustable Gastric Banding Syndrome. pH-Metric And Manometric Recordings in 19 Patients. *Mohamed Merrouche, Jean Marc Sabate, Pauline Jouet, Simon Msika, Severine Ledoux, Benoit Coffin*

Background: Adjustable gastric banding (GB) is one of the most common surgical procedure for the treatment of morbid obesity. However, GB frequently induces upper gastrointestinal symptoms. The consequences of GB on acid reflux and oesophageal motility have been poorly evaluated. The aim of this study was to describe pH-metric and manometric abnormalities in patients complaining of upper gastrointestinal symptoms after adjustable GB for morbid obesity. Patients and Methods: a standardized questionnaire, 24-hrs pH-metric recording (% of time with $pH < 4$) and esophageal manometry [lower esophageal sphincter pressure (LES), morphology, amplitude and propagations of oesophageal contraction waves] were performed in patients with GB addressed for upper gastro-intestinal symptoms and/or GB failure (insufficient weight loss) to a tertiary unit specialized in the treatment of morbid obesity. Results: (mean ± SD) 19 patients (F: 17; age 44.0 ± 10.2 yrs) were included 24 to 36 months after GB. BMI was 45.8 ± 6.9 kg/m² (range : 39.9-67 kg/m²) before surgery and 37.8 ± 9.2 kg/m² (range: 22.2-59.4 kg/m²) at the time of the study. Mean weight loss was 20.8±14.4 kg (range : 0-50 kg). None of these referred patients had had preoperative pH-metry or manometric recordings. At the time of the study, 13 patients (68.4%) had one or more upper gastrointestinal symptoms: vomiting more than 3 times a week in 9 (47.3 %), dysphagia in 6 (31.6 %), heartburn in 5 (26.3%) and epigastric pain in 3 (15.7%). pH-metry was abnormal in 6 out of 15 patients (40%) with a percentage of time with $pH<4$ of 29.5 ± 24.8 % (range: 8.5-71 %). Esophageal manometry was abnormal in 12 out of 19 patients with incomplete LES relaxation in 9 (47.4%) associated with abnormal oesophageal contractions in morphology, amplitude and duration; presence of non peristaltic waves were also noted. Conclusion: the presence of major reflux disease and oesophageal motor

disorders that could be defined as pseudo-achalasia are frequent in patients consulting for upper gastrointestinal symptoms and/or insufficient weight loss after adjustable gastric banding. These preliminary results in a small cohort of symptomatic patients without preoperative data suggest that complete oesophageal investigations are mandatory before performing bariatric surgery with adjustable GB, as it has been recommended before antireflux surgery.

212642: Pilot Study of Preoperative Weight Loss in Super Morbid Obese Patients: the Additional Effect of Endoscopic Intra-gastric Balloon Placement. *Gianluca Bonanomi, Simona di Caro, Mario Traina, Ilaria Tarantino, Giselle G Hamad, Madelyn H Fernstrom*

Background: Preoperative weight loss is often needed to reduce operative risk. Furthermore, adherence to dietetic and behavioral instructions is a determinant of patient compliance and outcome for bariatric surgery. Methods: Twenty consecutive patients suffering from super morbid obesity (BMI ≥ 50 kg/m²) were randomized for a 6-month balanced hypocaloric diet, either alone (group A) or associated with endoscopic intra-gastric balloon placement (group B). Mean age was 37.2 years (range: 21-55) in Group A and 38.9 (range: 24-58) in group B. Mean BMI was 56.5 kg/m² (range: 51-61) in group A and 58.4 (range: 50-69) in group B. There was no significant difference in age, BMI, gender, and comorbidities between the 2 groups. All patients received counseling and follow-up by a dietitian and were evaluated for possible bariatric surgery after 6 months. Results: Total mean weight loss after 6 months was 7 kg (range: 0-21) in group A and 19 kg (range: 8-32) in group B ($p < 0.05$). Mean % excess weight loss was 12% in group A and 32% in group B. Five patients in group A and no patients in group B experienced less than 5 kg weight loss after 6 months. One patient in group B developed pulmonary embolism that required early balloon removal. Nine out of ten patients with intra-gastric balloon and five out of ten patients on diet alone experienced a significant improvement of comorbidities and have undergone uneventful bariatric surgery. Patients who failed preoperative weight loss were submitted to additional dietetic and behavioral counseling or were referred for intra-gastric balloon placement. Conclusion: The results of this pilot prospective randomized study suggest that preoperative intra-gastric balloon placement in super morbid obese patients results in significant short term weight loss and comorbidities improvement as compared to diet alone.

220702: Rediscovered Therapeutic Option for Morbid Obesity: Multicenter Pilot Study with a New Pneumatic Stomach Balloon. *Yogesh Shastri, Irina Blumenstein, Udo Martin, Stephan Haass, Jurgen Stein, Wolfgang Caspary, Nicolas Hoepffner*

Background: Morbid obesity is a rapidly growing problem mainly of western society. Over 60% of the American population is either obese or overweight. Conventional treatment with reduced caloric intake, increased physical activity and pharmacotherapy are minimally effective in inducing sufficient weight loss, however the loss weight is often regained once the treatment is stopped. Given the comorbidities in these obese high risk patients, experienced bariatric surgeons often advocate a less invasive first stage intervention. The endoscopic implantation of various balloons in 80's and 90's could not come into vogue because of its associated complications. Since 2004 a new pneumatic intra-gastric balloon has come into practice. Ours is the first study reporting the safety, effectiveness, and tolerance of this new gadget in clinical practice. Patients and Methods: A pneumatic intra-gastric balloon system (heliosphere® bag, Helioscopie, France) was placed endoscopically 27 times in 24 patients in a multicenter pilot study since September 2004 till November 2005. They were followed up prospectively with data about symptoms, complications, loss of weight, BMI, etc. Results: There were 12 male and 12 females (age range 24-60, median 43 yrs) with a BMI range of 30-57 (median 37) and a body weight of 71-194 kg (median 113 kg). In 2 female and 1 male patients the procedure was repeated twice (after 5, 10 and 11 months). There were no procedure related complications. 16 (59%) of patients had balloon induced immediate side effects like occasional nausea with vomiting lasting 3 days in 6 patients (22%), 7 patients (32%) had more severe nausea, vomiting and abdominal pain, whereas 3 (11%) patients required admission and intravenous fluid administration for the same. In two patients we had to perform premature extraction of the balloons after 5 and 14 days of implantation because of intolerance and severe bleeding (Dieulafoy's ulcer) respectively. The remaining balloons were explanted 9 months (range 5 to 13 months) after implantation. Except for one patient all patients lost weight ranging from 1 to 29 kg with a fall in BMI ranging from 1 to 9. Conclusion: With this new found "old" technique the results are promising. It was efficient in inducing weight loss in mild or moderate obesity and can also be very useful for preoperative weight reduction as a first stage, low risk and less invasive procedure in morbidly obese patients.

216192: Intra-gastric Balloon for Refractory Obesity: Poor Compliance with Dietary Education and Follow-Up Does Not Preclude Weight Loss. *Erik Francois, Jean Marc Dumonceau, Marie Barea, Karine Buedts, Michael Piagnerelli, Jacques Deviere, Axel Hittlet*

Background: the intra-gastric balloon (IB) has been proposed as an aid to weight loss for patients with moderate obesity. By increasing satiety, the IB helps patients learn and adhere to new eating habits, which must be maintained after balloon removal if weight is to be stabilized. Thus, dietary education and follow-up before, during, and after IB placement are strongly recommended. Methods: From July 1999 to June 2004, 80 patients (68 women; body mass index, or BMI, range 28.4 to 58.5

kg/m²; mean±SD: 36.9±7.8) were treated with the BioEnterics® IntraGastric Balloon (Inamed corporation, Santa Barbara, California, USA), placed endoscopically under sedation with midazolam or anesthesia with propofol. Patients were screened by a dietician before placement, and monthly dietary follow-up was prescribed thereafter. Results: IB placement was successful and uneventful in all cases. Three patients were lost to follow up. One-year post-removal follow-up was obtained in 77 patients. One IB migrated spontaneously and 76 IB were removed endoscopically, 3 of which had spontaneously deflated while remaining in the stomach (spontaneous deflation rate: 5%). Early removal (<3 months) for intolerance was necessary in 14% of patients. The only other complication was one case of severe hypokalemia. Mean duration of IB placement was 180 days (range: 8 to 548 days). Mean weight loss at removal was 11.3 kg (±8.5 kg); mean % of excess weight lost (EWL) was 44.7% (±39.2%). Twenty-six percent of the patients lost less than 20% of excess weight. Six months after IB removal, the mean EWL was 26.2% (±40.3%) and was maintained at 22.4% (±58.5%) at one year. Weight loss was greater if BMI was >40 kg/m² (mean: 16.9 +/-13.2 kg) than if BMI was <35 kg/m² (mean: 10±6.6 kg) (p=0.01). Only 10 out of 80 patients were fully compliant with the prescribed dietary follow-up during IB and after removal. There was a trend to greater weight loss in the compliant group, but statistical significance was not achieved. Overall, 43% of the patients were satisfied with the IB. Conclusions: The IB appears to be safe and moderately effective in achieving sustained weight loss 1 year after removal despite poor compliance to dietary follow-up in this series.

226270: Markov Economic Model for Surgery in the Morbidly Obese. *Donald Garrow, Kit Simpson, Joe Romagnuolo*

Introduction: Gastric bypass surgery appears to be an effective tool for weight loss in the morbidly obese, but is an expensive procedure. Some insurance companies and government payers have been reluctant to fully fund this procedure. We sought to determine the cost-effectiveness of gastric bypass surgery in the morbidly obese. Methods: We used a Markov process to model progression of weight loss and associated costs for both surgical and non-surgical interventions. The base-case was a 50 year old patient with a body mass index (BMI) >40. A third-party payer perspective was used, using direct health care costs and indirect costs related to recovery from surgery. We included literature-derived data concerning BMI-specific direct costs (including physician visits, medication costs, hospitalizations, etc), transition probabilities, and quality of life (utilities), as well as competing age-specific death rates, for both laparoscopic and open gastric bypass surgeries versus diet and exercise with a decision tree. Indirect costs related to time lost recovering from surgery were considered. Transitions between BMI states were modeled in 1-year transitions, over a lifelong time horizon. Downstream health care costs and utilities were discounted at 3% per year. Incremental cost-effectiveness ratio (ICER) calculations were planned for non-dominant strategies. Results: Surgical therapy for obesity was dominant (less costly and higher quality of life), therefore an ICER is not calculable (no tradeoff). The discounted health care cost savings per patient over an expected lifetime for surgery vs. non-surgical therapy was \$21,248. However, the total procedure cost, ancillary services and hospital stay for the initial surgery took 13 years to recoup. Over the expected lifetime, 1.5 years (discounted) quality-adjusted-life-years (QALYs) were gained per patient for surgery vs. non-surgical therapy. Sensitivity analyses revealed the model conclusions to be robust. Conclusions: Surgery for the morbidly obese is a cost-effective (in fact dominant) choice for morbidly obese subjects when lifetime healthcare costs are considered.

221895: A Multi-Component Model Can Predict Outcome of Restrictive Surgery for Obesity at Baseline and 3 Months. *Naeem Aslam, Hani Rashed, Atul K Madan, David S Tichansky, Teresa Cutts, William D Johnson, Thomas L Abell*

Introduction: We previously reported that a multi-component model of autonomic and enteric factors may correlate with ultimate weight loss or gain after restrictive obesity surgery (NGM 2005; 17:472). Patients: We report on 39 patients, 4 male, 35 female, mean age 37.2 years, followed for up to 16 years post-operatively after vertical banded gastroplasty. Methods: Two autonomic measures (adrenergic: PAR and VC and cholinergic: RRI) and one enteric measure (electrogastrogram: EGG) were recorded at baseline as previously described (DDS 44: 74s-78s, 1999). We performed a discriminant function analysis to investigate whether a patient's EGG, PAR, RRI, and VC values could be used to classify that patient as a loser or gainer following weight control surgery. The patients were divided into two categories (10 gainers, 29 losers), depending on the latest weight compared to baseline; discriminant criterion derived from the patient's data was applied to each patient's autonomic and enteric values to determine whether these measurements separated the patients into their true weight category. Results: A discriminate model based on baseline measures successfully predicted ultimate weight gain in 8/10 (80%) of patients who subsequently gained weight and weight loss in 24/29 (83%) of patients who in subsequently lost weight for a total correct classification rate of 32/39 (82%). The same model with data at 3 months post-operatively predicted weight gain in 9 of 10 (90%) of patients and weight loss in 24 of 29 (83%) of patients, for a total correct classification rate of 34/39 pts (87%) (see table). Conclusions: A multi-component model demonstrates that baseline and 3 months post-operative measures can predict ultimate weight outcome from restrictive obesity surgery.

Time	Predicted Baseline	Outcome Lose	Total	3 Month Predicted	Outcome Lose	Total
Result	Gain	Lose	Total	Gain	Lose	Total
Gain	8 (80%)	2	10	9 (90%)	1	10
Lose	5	24 (83%)	29	5	24 (83%)	29

Four Component Model

Time	Predicted Baseline	Outcome Lose	Total	3 Month Predicted Gain	Outcome Lose	Total
Gain	8 (80%)	2	10	9(90%)	1	10
Lose	5	24 (83%)	29	5	24 (83%)	29

215054: Gastric Motor and Sensory Functions in Normal Weight, Overweight and Obese People. *Maria I Vazquez-Roque, Debra Stephens, Duane Burton, Kari Baxter, Michael Ryks, Matthew Clark, Michael D Jensen, Alan R Zinsmeister, Michael Camilleri*

Background: The literature on motor and sensory functions of the human stomach in relation to body mass presents contradictory information, in part because the functions have not been systematically studied in the same cohort of people. On the other hand, obesity is associated with several upper gut symptoms, and the mechanisms of symptom generation are unclear. In obesity, measured gastric volumes were normal except in the presence of bulimia (Physiol Behav 2004;81:735-40). Aim: To compare gastric volumes, emptying, maximum tolerated volumes (MTV) and post-challenge symptoms in normal, overweight, or obese volunteers who were otherwise healthy. Methods: We studied 68 of 72 participants in normal, overweight, or obese (WHO criteria) groups (all non-bulimic) and documented their lean mass and % fat by body composition (DEXA). All underwent the following measurements using validated tests: gastric emptying for solids and liquids by scintigraphy (GE t1/2); gastric volumes by SPECT, a validated imaging method (Gut 2002;51:781-6); MTV and 30 min post-challenge symptoms by satiation test (Neurogastro Motil 2002;14:249-53). Statistical analysis used one-way ANCOVA adjusted for gender. Results: The table summarizes the data, mean±SEM. There were significant differences in lean and fat mass and significantly lower fasting gastric volumes in the overweight and obese groups. We also observed borderline lower postprandial volume changes in obese and borderline faster gastric emptying of liquids. Conclusion: Being overweight or obese is associated with lower fasting gastric volumes, but there is no difference in food volume tolerated or symptom score after a challenge meal. The significance of lower fasting gastric volumes to upper gut symptoms in obesity requires further study.

	Normal weight (n=24)	Overweight (n=20)	Obese (n=24)	Overall p value
Age, y	37.4±3.0	36.6±2.0	44.3±2.6	0.11
BMI, kg/m ²	22.9±0.3	27.8±0.3	34.8±0.7	
Gender M:F	8:16	6:14	11:13	0.05
Lean mass	45593±1101	48200±1216	50607±1086	0.007
Tissue fat, %	30.6±1.2	39.9±1.3	47.7±1.2	<0.001
Fasting gastric vol, ml	258.7±13.1	198±14.7*	236.0±13.0**	0.01
Δ PP vol, ml	518.5±17.8	489.1±20.0	464.0±17.5\$	0.09
MTV, ml	1230.6±71.7	1197.7±79.1	1260.9±69.1	0.88
Aggregate symptom score	145.3±14.5	152.6±15.7	140.1±14.0	0.84
GE t1/2 solids, min	119.8±6.3	111.5±7.0	116.9±6.1	0.66
GE t1/2 liquids, min	26.3±2.5	19.4±2.9#	20.4±2.4#	0.13

Compared to normals: * p=0.003; ** p=0.055; \$ p=0.03; # p≤0.10

213927: Vagal Blocking for Obesity Control (VBLOC): Concordance of Effects of Very High Frequency Blocking Current at the Neural and Organ Levels Using Two Preclinical Models. *Katherine S Tweden, Mehran Anvari, Michael D Bierk, Charles J Billington, Michael Camilleri, Christopher N Honda, Mark B Knudson David E Larson, Richard R Wilson, James W Freston*

BACKGROUND: Vagal blocking using intermittent, very high frequency current is being studied for obesity management. The targeted physiologic effects are to: (1) inhibit gastric accommodation leading to early satiation and reduced food consumption; (2) inhibit gastric contractile activity leading to prolonged satiety; and, (3) inhibit pancreatic exocrine secretion (PES) leading to reduced calorie absorption. Historically, surgical vagotomy for refractory ulcers caused transient anorexia and weight loss by mechanisms that are unclear. **AIM:** To evaluate the effects of vagal blocking using intermittent, very high frequency current on pancreatic function and neural activity as measured by inhibition of PES and compound action potential (CAP) propagation, respectively. **METHODS:** In an acute porcine model using non-vagolytic (chloralose) anesthesia, electrodes were placed on the anterior and posterior vagal trunks at the esophagogastric junction. PES was measured by direct cannulation of the pancreatic duct. PES, as well as heart rate (HR), blood pressure (BP) and blood glucose, were measured before, during and after very high frequency vagal blocking at 5000 Hz. In an acute rat model, three pairs of bipolar hook electrodes were placed in series for stimulation, blocking and recording, respectively, on either the cervical vagus or sciatic nerves. The effect of block at 5000 Hz on the amplitude of electrically evoked fast and slow CAP waves was measured following 5 minutes of blocking at times 0, 1, 2, 3, 4, 5, 10 and 15 min post-block. Data are expressed as relative response (post-amplitude/pre-amplitude) x 100. **RESULTS:** Vagal blockade decreased PES >80% (0.35 ± 0.06 vs. 0.06 ± 0.01 ml/h, n=6, p=.005). PES returned to baseline values within 19 ± 8 min post-block. Immediately after block, CAP amplitude (fast and slow waves) was reduced to $3 \pm 2\%$ of baseline. CAP recovered to 50% by 2 min and 90% by 10 min (n=9). HR, BP and glucose remained unchanged. **CONCLUSIONS:** 1. Vagal blocking reversibly inhibits pancreatic exocrine secretion and compound action potential propagation. 2. The effectiveness of vagal blocking using very high frequency current was corroborated at the neural and organ levels in two preclinical models. 3. Physiologic changes caused by intermittent vagal blocking may offer potential for treating obesity without long-term loss of efficacy.