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Globesity, diabetes and surgery

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The obesity problem is a global epidemic of ever increasing proportions. Because of a number of different reasons many nations, in developed and developing countries, deal with this problem. While the U.S.A. stand in "pole position", in Europe the uncontrolled diffusion of sweet snacks is responsible for children obesity, in China the diminished numbers of bikers in favour of car drivers, in Oceania the success of "fast food" instead of the traditional fruit consumption are considered as causes of this phenomenon.

All in all, according to reliable statistics, 1.5 billion people all over the globe are obese: globesity.

Taking care of all these people accounts for 2-8% of all the national medical expenses, as much as it takes for all tumours, with the added difference that expenses for obesity grow by 25 % every three years.

Further, mortality for obesity is three times the compounded mortality of colon and breast cancers.

Obese individuals have a life expectancy approximately shortened by 10-15 %, because of diabetes, cardiovascular diseases, hypertension, cancer etc. One important and undervalued problem is the augmented frequency of many different malignant tumours found in the USA and Canadian obese population as reported in the "New England Journal of Medicine" and found by us in the Italian obese population

Surgery in obese patients may reduce sanitary costs by 45% after 5 years. U.S.A. statistics show that, three years and a half after surgery, operated patients cost less than non operated patients.

At the same time mini invasive laparoscopic surgery, during the last 20 years, has had a tremendous diffusion world wide.

The combination of these two factors, obesity and laparoscopy, determined a "critical mass" which resulted in the explosion of bariatric surgery, with an exponential growth in the last 10 years. The advantages of laparoscopic surgery were greatly stressed in bariatric surgery.

Early mobilization and early recovery of G-E functions,

peculiar to laparoscopic surgery, are advantageous to all patients but, even more so, in morbidly obese patients which are high risk patients.

The great compliance of patients to bariatric laparoscopic surgery caused in the U.S.A. a jump from 10.000 procedures per year from the seventies to the nineties in the last century, to 250.000 procedures during the last year.

Standardization of surgical techniques was an added reason for the success of laparoscopy. The EAES Consensus Conference in 2004 and the Consensus Statement of ACS in 2005 indicated 4 types of standard surgical procedures: adjustable gastric banding, vertical banded gastroplasty, gastric by-pass, bilio-pancreatic diversion.

Indications to surgery must be based on reasonable expectations from the surgeon and from the patient. On this regard the psychiatric/psychological interview is of the utmost importance to avoid vain hopes and bitter disappointment. At present internationally accepted and established precise criteria must be considered to indicate bariatric surgery.

Once surgery is indicated, which kind of operation should be chosen? Over the years, many different procedures, with a variety of rational basis, have been proposed.

The first significant contribution of surgery to the solution of the obesity problem was the intestinal bypass proposed and performed by Linner, Kremer and Nelson in 1954. In 1963 Payne standardized the jejunal-ileal by pass. The procedure determines a very effective and indiscriminate malabsorption by reducing to 30 cm the functioning (digestion and absorption) small intestine.

However the early and unquestionable effect of surgery was due to very significant physio-pathological changes with severe side effects, in particular severe liver sequelae, even cirrhosis. All major surgical societies consider this procedure *banned*.

At present there are three groups of standard surgical procedures, internationally accepted:

– *restrictive procedures*, laparoscopic adjustable silicone gastric banding (LASGB) and vertical banded gastroplasty



(VGB); – *malabsorptive procedures*, bilio-pancreatic diversion (BPD and its modification with the so-called “duodenal switch” (BPD-DS); - metabolic procedures, gastric by pass (GBP).

VBG, once the procedure of choice, is almost completely abandoned in the U.S.A., and is in declining popularity in Europe.

LASGB was the first bariatric procedure to be performed by laparoscopy and it is now the most frequently used in Europe, with over 150.000 cases.

The reasons for LASGB popularity are: - it is a simple procedure with very few operative and post operative complications; - it is easily reversible, in most cases by laparoscopy; - it is effective in 70% of cases and even more when selection of patients is very accurate.

L.A.S.G.B. on one hand presents the lowest incidence of operative and post-operative complications, but it has the highest incidence of late complications requiring a surgical procedure.

Major complications are: *band migration* into the stomach due to erosion of the gastric wall; *pouch dilatation* due to slippage or technical faults. However these complications almost always do not represent emergency situations and are dealt electively.

The treatment for the gastric pouch dilatation is the complete band desufflation (conservative treatment), followed by a progressive insufflation. The failure of the conservative treatment makes it necessary to reposition or to remove the prosthesis. To prevent this kind of complication it is better to create a virtual pouch above the “bursa omentalis” and to fix the prosthesis using gastro-gastric sutures.

The incidence rate of the gastric erosion is between 1,6% and 6,3%, considering several clinical experiences. Solution in most cases is mini invasive surgery: laparoscopic, endoscopic or combined laparoscopic-endoscopic.

Clinical results, after LASGB, are considered satisfactory (BMI below 35) in 70-80 % of cases. The best results are obtained in non super obese young women without alimentary disorders like BED or sweet eating.

GBP represents 70% of all bariatric procedures in the U.S.A.

GBP determines a EWL of 60% in the long period (over 14 years), cures co-morbidities like diabetes, hypertension etc. in 80-90% of cases and has a low re- intervention rate. For all these reasons GBP in the USA is considered the gold standard in the treatment of morbid obesity.

Complications of GBP include haemorrhage (0.8-3.8%), fistulization (0.8-3.6%) and strictures (1.6-5.8%), mainly involving the gastro-jejunal anastomosis in the immediate postoperative period.

In the long run internal hernias occur with an incidence between 0.6 and 6% in different literature reports. The pathogenesis is due to the incarceration of small bowel in the surgery induced mesenteric defects, which become more hazardous when visceral fat diminishes significantly.

The mechanism of action of this procedure involves gastric restriction during the first post-operative period. However the two main patho-genetic factors are: decreased appetite and increased satiety which are tied to the hormones ghrelin produced by the stomach and PYY, stimulated by early arrival of non processed food to the ileum. The alimentary exclusion of the gastric body and fundus determines low levels of ghrelin, hormone of appetite, and flattens its circadian rhythm: hunger and daily meals frequency are reduced.

During the last few years great attention has been given to the anti-diabetic effect of GBP. This effect has a very rapid onset and is independent from weight loss suggesting the presence of a hormonal mechanism.

Two mechanisms have been hypothesized: the Foregut hypothesis and the Hindgut hypothesis.

In 1998 Paries foresaw a role for the duodenum-jejunum in the pathogenesis of diabetes mellitus (2 D.M.).

In 2004 Rubino and Gagner pinpointed a number of early hormonal effects of GBP.

In 2006 again Rubino elucidated, experimentally, the role of duodenal exclusion in controlling 2 D.M. hypothesising the presence of an anti-incretin substance secretion.

According to the hindgut hypothesis unmodified food reaching the terminal ileum stimulates ileum L-cells to secrete GLP – 1.

Finally the two main types of malabsorptive procedures are: BPD and BPD – DS.

BPD was conceived in 1972 and performed in man in 1976 by Scopinaro.

In extreme synthesis Scopinaro obtained a high malabsorptive effect with minimal malnutrition consequences.

Patho-physiology of BPD is related to two factors: - a 50 cm common channel where mixing of food with the bilio-pancreatic secretion occurs with diminished fat absorption and diminished caloric intake; - a 200-250 cm alimentary channel in which proteins, calcium and glucids are absorbed lessening malnutrition problems.



In 1988 Scopinaro procedure was modified by Hess to reduce the occurrence of possible troublesome diarrhoea symptoms. Main differences are: sleeve gastrectomy with pylorus maintenance, 100 cm common channel: BPD-DS.

Further Gagner proposed a two steps procedure: first the sleeve gastrectomy. After an interval of 6-12 months and a significant EWL, the second step is performed. The two steps procedure significantly reduces morbidity and mortality when compared to the one step procedure.

BPD determines a 50-75 % EWL at long (>10 years) follow up, being the most effective procedure on excess weight. Similarly this procedure is very effective on the metabolic syndrome (diabetes mellitus 2: 90/100 % resolution, hypercholesterolemia 100 % resolution, etc.

Complications of BPD are: bleeding (6 %), fistulization (2 %), pulmonary embolism (0.5 %) and respiratory problems. In most instances the treatment is conservative. Anastomotic ulcers occurrence has been greatly reduced by proton pump inhibitors therapy.

Specific side effects of BPD include: tiredness, gas bloat syndrome, peripheral oedema and, most undesirable, diarrhoea (15-20 %) with foul smelling stools.

According to Hess and to Gagner BPD-DS seems to decrease the incidence of these side effects due to the longer common channel (100 vs 50 cm) and to the maintenance of the pylorus.

Before closing on surgical procedures, only few words on an old technique with novel interest. In the last few years the intra-gastric balloon (BIB) has had an ever increasing popularity among patients and surgeons due to the ease of application (endoscopy in sedation), and to encouraging results.

BIB has been used primarily in the treatment of borderline cases and as a preoperative procedure to decrease operative risks.

A randomized study showed that the BIB induced weight-loss is not a placebo effect but is dependent on a specific mechanism. BIB induced in 80% of cases a significant improvement of respiratory function and sleep apnoea episodes.

One problem we are confronted with is the indication of the type of surgery in the individual patient. In the Nice 2000 EAES consensus conference suggestions have been given. The criteria adopted take into account well established data. Although all the three main surgical procedure, more commonly executed, determine a significant EWL, this effect increases from LASGB, to GBP, to BPD. Two additional factors taken into consideration are: existence of co-morbidities

and psychological profile of alimentary behaviour. Unfortunately, at present, precise and very reliable criteria do not exist. The last word is always to the patient and to his satisfaction.

In conclusion bariatric surgery determines an effective and long term EWL with a beneficial effect on co-morbidities. As a consequence life expectancy is lengthened and quality of life is ameliorated. The social-economic impact is very effective.

Key points are: correct selection of patients, adequate surgical technique, and exhaustive follow-up.

The laparoscopic approach is, by no means, the gold standard as it fulfils all criteria to be considered so: safety, efficacy, reproducibility, cost effectiveness. The efficacy at the 10 years follow-up will, we are certain, confirm the present results.

However there are a number of controversial "hot topics" related to:

- **age**, both for the adolescent and for the elderly; **weight limits** (class 1 obesity) for indication to surgery; - criteria for **selection** of the type of surgery in the individual patient; - **diabetes**; - **sleeve gastrectomy**.

In the last few years age limits both on the upper and on the lower range are under debate. Obesity is extending to surprising new categories of individuals. Particularly worrisome is the phenomenon in the paediatric age with percentages that go as up as 20-25% between 9 and 12 years of age. Italy holds first place in Europe, together with Greece. Fifteen per cent of these children eventually will be morbidly obese adults.

Debate exists also for weight limits (class 1 obesity), since the ever increasing demand for surgery.

Among the "hot topics", diabetes and its relationship with obesity is, at present, the hottest. In the world there are 190 million diabetes mellitus patients, 90% of which are obese. "Diabetes" is the XXI century epidemic

GBP and BPD seem to exert an anti-diabetic effect, independently from the weight loss, determined by an endocrine mechanism in part clarified, but still needing further investigation.

The anti-diabetic effect of GBP and BPD is so relevant that Dixon, in a momentous editorial strongly suggested a role for surgery in the therapy of DM 2.

The goal of a surgical therapy for diabetes is pursued by many surgeons around the world. Trials are ongoing in Europe, U.S.A. and South America. In the "Diabetes Surgery Summit (DSS)", that took place in Rome in March 2007, the top medical and surgical authorities from all over the world



joined to put the basis for future investigational and clinical studies. The impact of the summit was such that the American Society of Bariatric Surgery (ASBS) has decided to change the name to ASM(etic)BS. A similar decision was taken by the Italian and other obesity surgery societies.

Diabetes surgery is nowadays a developing reality.

We retrospectively reviewed the results of 110 obese diabetic patients, who underwent laparoscopic gastric banding or gastric by-pass or sleeve gastrectomy with a mean follow up of 24 months. Regardless of the type of surgical procedure, bariatric surgery cured diabetes in 76, 3% of these “diabetes” patients. In April 2007 Cohen et al. reported the preliminary data on two diabetic patients with BMI of 22 and 34 Kg/m², surgically treated with a duodenal-jejunal by-pass. Patients had normal blood glucose levels 5 weeks after surgery and were off anti diabetic drugs.

An endo luminal technique has been proposed recently: a prosthesis (60 cm in length) is anchored to the duodenal bulb, so preventing contact of ingested food to the duodenal-jejunal mucosa. The ingested food is separate from bilio-pancreatic juices for all the length of the prosthesis, mimicking a surgical duodenal-jejunal by-pass. Preliminary results on the resolution of glucose metabolism alterations are highly promising.

The enthusiasm is great and, may be, a word of caution may seem appropriate.

In the last few years sleeve gastrectomy (or vertical gastrectomy) performed as first step in DS, stimulated a novel approach to obesity surgery, being proposed by a number of surgeons as a “solo” procedure.

In a recent summit, in New York City, the results of sleeve gastrectomy on excess weight and on co-morbidities after a follow-up of 3 years, have been reported. In collect reviews (775 patients) the results in terms of EWL (between 33-83%), morbidity (14%), mortality 0.4 % and the reduction of co-morbidities were very promising. Disadvantages of sleeve gastrectomy are: irreversible procedure, postoperative complications at a very low frequency but, when present, at high risk. The advantage is that in patients with non satisfactory results, a second step procedure may be performed with diminished operative risks. The second procedure may be multidirectional: D.S. or gastric by pass have been equally adopted, with relative technical ease.

At present, clinical results of sleeve gastrectomy, as a “primary solo” procedure, in the treatment of morbid obesity, encourage to pursue on this path. The American Society for Metabolic Bariatric Surgery (ASMBS) gave out a statement

defining sleeve gastrectomy a suitable “option” in the treatment of morbid obesity “in particular in patients at high preoperative risk or in super-super obese patients”. In these instances sleeve gastrectomy can be considered a “risk reduction strategy”.

As far as indication for a “tailored” type of operation in the individual patient, in 2007 we are still in the *stone age*. We need criteria that should take into account: behavioural index, metabolic index, genetic codex and, possibly, allow us to indicate more correctly and properly what is the best surgical treatment in the specific patient.

On the other hand therapeutic trials are difficult for a number of reasons: different social environments determine different economic conditions, different alimentary habits and different surgical experiences. Further different genetic factors and the validation criteria necessitating a long follow-up period make the goal even harder to achieve.

Obesity, appropriately defined “globesity” is, to all accounts, a social problem. All components of *society must take the burden*: - *the teaching institutions* with an adequate nutritional education; *the National Health System*, with effective preventive campaign, as it has been done for smoking, and with specific outpatient structures for pre and post-surgery care; - *the media* with a correct information avoiding misleading stories on the so called “malpractice”; - finally *politicians* who should not behave like the proverbial three monkeys: I do not listen, I do not see, I do not talk.

Where are we going and where is the future?

In the last two decades surgeons have been constantly pursuing the “mini-invasiveness”. On this path another prestigious enterprise has started: Natural Orifice Transluminal Endoscopic Surgery (N.O.T.E.S.). Trans vaginal, trans gastric cholecystectomies and appendectomies have been performed, intra gastric per-endoscope procedures have been realized by means of endoscopic suturing devices. In bariatric surgery the first experimental models of restrictive procedures have been realized. The road is open for exploration.

Will surgery be the ultimate weapon against obesity? Probably it will not. We are already trespassing from the genetic engineering (building *with genes*) to the genetic factory (building *the genes*). May be, sometimes in the future we will go from the laparoscopic *mini-invasiveness* to the *non invasiveness*.

In prehistory of man, obesity was a defensive factor, helping the individual to survive through cold winters and famine. Today obesity has become a global dramatic risk for man. Surgery seems to confront effectively with the problem.

