MINERVA CHIRURGICA

VOLUME 71 · No. 2 · APRIL 2016

EDIZIONI · MINERVA · MEDICA

PUBBLICAZIONE PERIODICA BIMESTRALE - POSTE ITALIANE S.P.A. - SPED. IN A. P. D.L. 353/2003 (CONV. IN L. 27/02/2004 N° 46) ART. 1, COMMA 1, DCB/CN - ISSN 0026-4733 TAXE PERÇUE

The online version of this article is located at http://www.minervamedica.it
Minerva Chirurgica 2016 April;71(2):114-23

REVIEW

New devices for the bariatric patient

Isabelle DEBERGH [1]*, Christophe SNAUWAERT [2], Bruno DILLEMANS [1]

[1]Department of Surgery, AZ Sint-Jan AV Brugge/Oostende, Campus Brugge, Brugge, Belgium; [2]Department of Gastroenterology, AZ Sint-Jan AV Brugge/Oostende, Campus Brugge, Brugge, Belgium

*Corresponding author: Isabelle Debergh, Department of Surgery, AZ Sint-Jan AV Brugge/Oostende, Campus Brugge, Ruddershove 10, B-8000 Brugge, Belgium. E-mail: Isabelle.Debergh@azsintjan.be

ABSTRACT

Over the past years, the global prevalence of obesity has risen dramatically. This generates enormous costs for the health care system, since obesity is associated with hypertension, diabetes mellitus type 2, coronary heart diseases, stroke, dyslipidemia, psychological problems, and cancer. Bariatric surgery has demonstrated to be the most effective and durable treatment option in the morbidly obese patient. Despite its evidence based efficacy, less than 1% of obese patients will undergo surgery. The role of new, less-invasive devices for the bariatric patient needs to be defined. Are they situated in the gap between lifestyle modification and surgery for the obese patient, in the preoperative work-up of the super-obese patient, in patient groups that are currently excluded for surgery, and/or in the routine treatment of obesity as a chronic disease? This review will focus on emerging technologies for the bariatric patient that are currently in clinical practice or in an advanced development stage, with different modes of action: inducing stretch on the gastric wall (space-occupying or stitching devices), vagal neuromodulation, altering the absorption, or exclusion of the duodenum and proximal jejunum. Exploring the evidence and the indication of different therapeutic approaches and innovations will be an interesting field of research in the near future.

(*Cite this article as:* Debergh I, Snauwaert C, Dillemans B. New devices for the bariatric patient. Minerva Chir 2016;71:114-23)

Key words: Obesity - Bariatric surgery - Surgical procedures, operative.

Worldwide, the prevalence of obesity has risen dramatically over the past decades. On society level, the health care system is burdened heavily with this problem, since obesity is associated with increased rates of non-communicable diseases, such as hypertension, diabetes mellitus type 2, coronary heart disease, stroke, dyslipidemia, cancer, psychological problems and eventually mortality.[1] Projections for the near future suggest that the trends in obesity will lead to declines in life expectancy.[2] The World Health Organization (WHO) signalized already in 2000 the trends in the global epidemic of obesity, and developed prevention and management strategies.[3] So far no country was found where a decrease in prevalence of overweight or obesity was reported over the past three decades. A recent global systematic analysis stated that the proportion of adults with a BMI of 25 or greater increased from 28.8% in 1980 to 36.9% in 2013 for men, and from 29.8% to 38.0% for women.[4] These trends are similar in developed and developing countries, and among children and adolescents. The declaration of the WHO members to halt the rise in obesity by 2025 shows of a great ambition,[5] and should be embedded in a visionary health care system, with attention for preventive measures on societal level, and lowering the threshold for therapeutic interventions for the individual, whether a conservative or invasive treatment is applicable. Bariatric surgery has demonstrated to be the most effective and du-

rable treatment option in the morbidly obese patient.[6] Despite its evidence based efficacy, less than 1% of obese patients will apply for surgery.[7] The reasons for this are divers, including hospitalization costs, patient reluctance, access to health care, surgical morbidity or mortality risk. The role of less-invasive therapies and innovative devices can be situated in the gap between solely lifestyle modification and surgery for the obese patient, in the preoperative work-up of the super-obese patient, in patient groups that are currently excluded for surgery, such as children and adolescents, and in the treatment of obesity as a chronic disease, for instance failed bariatric surgery. This review will focus on emerging technologies and new devices for the bariatric patient, which are currently used in clinical practice or in an development stage. Having more safe and reliable treatment options, and improving the outcome of bariatric surgery as an entity is the final goal to fight the obesity pandemic.

Inducing stretch on the gastric wall

One of the most frequent used strategies in weight loss surgery is increasing the restriction capacities at the level of the stomach, such as placing the laparoscopic adjustable band, the sleeve gastrectomy or the accomplishing of a small gastric pouch in the Roux-en-Y gastric bypass (RYGB). The induction of early satiety and the stretch on the small gastric reservoir alters gastric emptying and induces orexigenic hormones.[8] This principle forms the base of the intragastric restrictive devices.

Space occupying devices

In 1985, the first endoscopically placed intragastric balloon for the treatment of obesity was introduced with the Garren-Edwards gastric bubble. Unfortunately, this balloon failed to demonstrate efficacy in a prospective, double-blind, randomized trial, following 59 obese patients over a 9-month period.[9] Also, serious adverse events were reported, including gastric mucosal damage and small bowel obstruction after balloon migration, necessitating surgical intervention. After withdrawal from the market, the Orbera intragastric balloon was launched (Apollo Endosurgery, Austin, TX, USA). This endoscopically placed silicone balloon can be filled with 450 to 700 mL saline and methylene blue dye to ensure early detection of leakage, by changing the color of the urine. Normally, after 6 months the balloon has to be endoscopically removed. The Heliosphere BAG (Helioscopie, Vienne, France) is a similar balloon system, to be filled with 950 mL of air, instead of fluid.

The ReShape Duo (ReShape Medical, San Clemente, CA, USA) is a combination of 2 independent balloon systems, which can be filled with 450 mL saline and methylene blue per balloon during an endoscopy session. An extraction after 6 months is also recommended.

The Spatz Adjustable Balloon System (Spatz Medical, Great Neck, NY, USA) is a special variant, allowing endoscopic adjustment of the instilled volume of saline. It is approved for 12 months of implantation.

To skip the endoscopic placement of a balloon, the Obalon gastric balloon was developed (Obalon Therapeutics Inc, Carlsbad, CA, USA). A large gelatin capsule contains a balloon, with a thin catheter to a self-sealing valve. After swallowing the capsule, the balloon will be freed in the stomach, and the catheter will allow the inflation of gas. Maximally 3 capsules can be ingested, and all balloons must be endoscopically removed after 12 weeks. The Elipse balloon (Allurion Technologies, Wellesley, MA, USA) was not only developed to be ingested without the need for endoscopic placement, retraction is not necessary. This balloon is also placed in a capsule, which will be digested in the stomach, and the balloon will be filled with 550 mL of saline through a catheter. After a certain period of months, the balloon will empty and spontaneously be excreted through the bowel.

To specifically delay gastric emptying, the

TransPyloric Shuttle (BAROnova Inc., Goleta, CA, USA) was designed. This system contains two bulbs, of which the larger one will prevent migration through the pylorus, and the smaller connected bulb will advance into the pylorus and the duodenum. Each peristaltic movement of the stomach will seal the pylorus, slowing down gastric emptying, and inducing early and prolonged satiety.

The space-occupying capacities of a balloon, can be mimicked with a pill containing hydrogel particles that are released from the Gelesis100 capsule (Gelesis, Boston, MA, USA). These particles will expand in the stomach by absorbing water and enhancing satiety through the volume effect. Preliminary results show that Gelesis100 is expected to reduce weight with 4.5% over 3 months combined with dietary measures, according to information on the producer's website. Unpleasant side-effects described in patients were bloating, flatulence, abdominal pain, and diarrhea correlating with the dose of the product.

Pressure on the gastric cardia can induce satiety, and this can be also mimicked with the Full Sense Device (BFKW LLC, Grand Rapids, MI, USA). This modified covered gastroesophageal stent has a cylindrical esophageal component and a gastric disk which can be placed and removed endoscopically.

Early satiety can also be induced by slowing down the duodenal transit -altering the satiety hormone levels- through placing the SatiSphere (Endosphere, Columbus, OH, USA) which is a memory wire covered by several mesh spheres, into the distal stomach and duodenum.

Results

Different studies report on the safety and efficacy of all intragastric restriction devices. In a meta-analysis of 1683 patients, the % excessive weight loss (%EWL) with the Obera balloon at 12 months was 25.44%, with a mean difference in %EWL over controls of 26.9% ($P \leq 0.01$) and $\leq 5\%$ incidence of serious adverse events, which was an acceptable safety profile.[10] Almost all study protocols combine Orbera balloon therapy with lifestyle modification or pharmacotherapy. Decreases were also noted in the incidence of comorbidities, such as type 2 diabetes mellitus, hypertriglyceridemia, hypercholesterolemia, hypertension, osteoarthropathy, obstructive sleep apnea, and nonalcoholic steatohepatitis after 6 to 18 months, even up to 3 years after the Orbera balloon insertion.[11-14]

The role of the Orbera balloon as bridge therapy to bariatric surgery has carefully been examined in super-obese patients. A decreased operative time, fewer intraoperative adverse events, and shorter hospital stay were reported in 2 matched case-control studies[15-16] although others notice no additional advantage compared with a preoperative professional weight loss program[17].

In a review of 8500 patients, pain and nausea are frequently described adverse effects after Orbera balloon implantation (33.7%), for which medical treatment can be prescribed. 18.3% of patients report GERD, and 12% suffer from gastric erosion. Early removal of the balloon was necessary in 7.5% of the patients. Balloon migration was reported in 1.4% of cases with small bowel obstruction in 0.3%, and gastric perforation in 0.1% of the subjects (mostly after previous gastric surgery).[18] A nonrandomized study comparing the Heliosphere BAG (N.=13) with the Orbera balloon (N.=19), revealed better weight loss results in the Orbera balloon group, but one mortality in the Orbera group 13 days after placement.[19] Balloon extraction was reported to be more difficult in the Heliosphere BAG patients.

The efficacy concerning weight loss of the ReShape Integrated Balloon System was investigated in the REDUCE pivotal trial with 326 obese patients randomized in the balloon group, or in the sham endoscopy group. Both groups were supported with dietary measures and exercise program during a period of three months, in which a 27.9% EWL was seen in the balloon group, and 11.3% EWL in the control population. Complications included balloon deflation (6%) without migration, early retrieval for nonulcer intolerance (9%), and

gastric ulcers and erosions (35%) positively evolving after device adjustment (10%).[20] Serious adverse events were observed: one esophageal mucosal tear, one contained cervical esophageal perforation and one post-retrieval aspiration pneumonitis.

Evidence about other intragastric balloons is poor. Two non-controlled studies evaluated the effect of the Spatz Adjustable Balloon system in 94 patients, where % EWL at 1 year was reported to be 46%.[21, 22] The TransPyloric Shuttle was also tested for 3 or 6 months in a small non-controlled trial,[23] including 20 patients with BMI 36.0 kg/m². Three-month patients ended up with 25.1% EWL, and 6-month patients with 41.0% EWL. Early device removal was necessary in 2 patients caused by gastric ulceration.

Results of the SatiSphere in 21 patients were compared to 10 control patients, showing 6.7 kg weight loss in the SatiSphere group versus 2.2 kg weight loss after 3 months in the controls.[24] In 10 individuals, a device migration was observed, and in 2 patients emergent surgery was necessary.

Endoscopic gastric suturing devices

The endoscopic sleeve gastroplasty (ESG) is a gastric volume reduction therapy in which 8 to 14 endoluminally placed full-thickness sutures are placed starting from the prepyloric region to the gastroesophageal junction with the OverStitch suturing device (Apollo, Endosurgery, Austin, TX, USA), appositioning the anterior and posterior gastric wall but without performing a plication. Similarly, the EndoCinch and RESTORe device (Davol, Murray Hill, NJ, USA) are a superficial- and full-thickness endoscopic suturing system respectively, which use suction to position tissue in a hollow capsule, and then suture the tissue with a needle going through the capsule.

To perform a transoral gastroplasty with staplers, the TOGA or TransOral GAstroplasty device (Satiety Inc, Palo Alto, CA, USA) can be used. This flexible endoscopic stapler is capable of full-thickness tissue apposition along the lesser curvature and uses vacuum to position the gastric wall. A similar type of stapler device is the ACE stapler (Boston Scientific Corporation, Natick, MD, USA) to place 8 plications in the fundus, and 2 in the antrum.

Endolumenal gastric plication instead of the sleeve gastroplasty, can be accomplished with the Primary Obesity Surgery Endolumenal (POSE; USGI Medical, San Clemente, CA, USA) platform to place transmural tissue anchor 8 to 10 plications in the gastric fundus and in parts of the distal gastric body.

Unlike the previously mentioned procedures, gastric restriction can also be obtained by implanting a diaphragm in the resized stomach. Implantation of the Transoral Endoscopic Restrictive Implant System (TERIS; Barosense, Menlo Park, CA, USA) is a restrictive intervention making a small gastric pouch by placing 5 anchors in the plicated stomach wall, and attaching this diaphragm to it.

Results

The feasibility and safety of the gastric suturing techniques are under review in different ongoing prospective trials. So far, 2 small studies with 20 and 10 obese patients evaluated the ESG intervention, and reported a % EWL of 30 and 40% at 6 months, respectively.[25, 26] Another study at the Mayo clinic followed 25 patients undergoing the ESG, with reported 53%, 56%, 54%, and 45% of EWL after 6, 9, 12, and 20 months respectively.[27] Three patients had serious adverse events (a perigastric inflammatory collection, a pulmonary embolism, and a small pneumothorax), but made full recoveries.

A study of transoral gastroplasty in 64 patients using the EndoCinch device reported a 58.1% EWL after 1 year, and no serious adverse events.[28] Moreover, in 21 adolescents (age 13-17) with an average BMI of 36.2 kg/m², a decrease of the excessive weight was seen towards 67.3% EWL after 1 year and 61.5% EWL after 1.5 year.[29] After the modification towards the RESTORe, a two-center trial was set up including 18 patients. No sig-

nificant complications were noted, and 1-year % EWL was 27.7%.[30] Unfortunately, follow-up endoscopy showed partial or complete release of the plication in 13 patients.

TOGA was studied in 21 patients (mean BMI 43.3 kg/m²) and showed no serious adverse events, an average of 24.4% EWL after 6 months, but staple line gaps in 13 patients during follow-up[31]. A multicenter study of 67 patients reported 41.3 to 52.2% EWL after one year and improvements in hyperlipidemia and glycemic regulation,[32] while a smaller series of 29 patients showed 14.9% total body weight loss.[33]

Early results of 17 patients undergoing an endoscopic gastroplasty with the ACE stapler, showed self-limiting nausea and vomiting after the procedure, a 34.9% EWL and 6-9 plications on endoscopic control after one year.[34]

A prospective trial including 45 obese patients after the POSE procedure, revealed 49.4% EWL at 6 months.[35] Long-term follow-up of 147 patients up to 1 year after the POSE procedure, showed a sustained % EWL of 44.9% [36] and an improved glucose homeostasis with positive influences on satiation peptides (ghrelin, PYY).[37]

A small pioneer study including 13 patients with TERIS described %EWL of 22.2% after 3 months, one gastric perforation, and two cases of pneumoperitoneum.[38]

Besides the utility of using endoscopic suturing or plication devices as primary solution in obese subjects, they were considered as an attractive option for reinterventions on failed bariatric procedures. Gastrogastric fistulas could be closed, or a voluminous gastric pouch or an increased diameter of a gastrojejunostomy in a failed gastric bypass could be treated with endoscopic revision devices. The effectiveness of EndoCinch for performing a TORe (transoral outlet reduction) in revision of a gastric bypass was recently investigated. No major adverse events were reported, and early results revealed a total body weight loss of 3.8% in the TORe group compared to 0.3% in the control patients, and a 4.4 kg of weight loss after 6 months.[39, 40] The full-thickness stitches with the OverStitch device showed more favorable results after 6 months, with an average weight loss of 10.6 kg in treated patients.[40] Revision of the gastric bypass with full-thickness stitches showed 20.0% EWL at 2 years, and 19.2% EWL at 3 years.[41]

The POSE was specifically adapted for revision of gastric bypass, called ROSE (Revision Obesity Surgery Endolumenal). This allows plication of the gastric pouch or the gastrojejunostomy, and was successfully applied to 97% of cases without having serious procedural complications in 116 patients investigated in a multicenter trial.[42] When gastrojejunal aperture decreased to 10 mm, patients experienced a 24% EWL after 6 months.

StomaphyX is a similar full-thickness plication platform (EndoGastric Solutions, Redmond, WA, USA), and was investigated in different studies proving to be safe and feasible, and revealing a 11.5% EWL after 6 months and 19.5% EWL after 12 months.[43, 44] A randomized controlled trial of StomaphyX versus sham procedure for revision of failed gastric bypass, led to early termination of the study as the primary endpoint, which was decrease of the pre-RYGB excess weight by 15% or more excess BMI within one year, was not met in more than 50% of the enclosed subjects.[45] Handling pouch dilation in failed VBG, showed to be safer with endolumenal pouch reduction with Stomaphyx compared to revision of gastric bypass, but less effective in terms of weight results.[46]

Vagal neuromodulation

Vagal nerve signaling has been linked to the delay in gastric emptying and experiences of hunger and satiety, and is thought to have a role in energy metabolism and upper gastrointestinal tract function. The vBloc neurometabolic therapy (EnteroMedics, St Paul, MN, USA) is delivered by a pacemaker-like device called the Maestro Rechargeable System. This laparoscopically implanted device delivers high frequency, low energy electrical impulses to the vagal nerve, on the anterior and posterior side of the stomach.

Results

The EMPOWER Study, a randomized controlled double-blinded trial performed in 2012, has proven a % EWL of 17% in the vBloc group (N.=192) after 12 months, but not statistically significant different to the control group (N.=102).[47] More recently the group of Billington[48-50] observed in the ReCharge trial a % EWL of 25.8% after 12 months, of 24.4% after 15 months, of 23.5% after 18 months, and of 22% after 24 months of vBloc therapy (N.=162), which was significantly better than the control group (N.=77). A better glycaemia control and lower systolic blood pressure were described, and the most common adverse events were mild or moderate heartburn, implant site pain, and constipation.

Altering the absorption

The AspireAssist (Aspire Bariatrics, King of Prussia, PA, USA) is a type of percutaneous gastrostomy which is endoscopically placed, and allows aspiring stomach contents.

Results

A pilot study allocated 11 patients to AspireAssist therapy, and 7 patients to the control group. After one year, a combination of conservative measures (such as dietary and behavioral modification) led to an 18% reduction of the total body weight in the AspireAssist group compared to 5.9% in the control patients[51]. More recent, a non-controlled study examined 22 patients for 6 months after placement of the aspiration therapy, diet and cognitive behavioral therapy, and reported 40.8% EWL.[52]

Exclusion of the duodenum and proximal jejunum

The EndoBarrier duodenal-jejunal bypass liner (GI Dynamics, Lexington, MA, USA) consists of an anchor placed in the duodenal bulb and a 60 cm polymer sleeve bypassing the duodenum and proximal jejunum. In this way, contact between food and biliopancreatic secretions is delayed and allows food to enter the midgut earlier. The principle of excluding the proximal small intestine will lead to weight loss mediated by changes in hormones that alter appetite, such as a postprandial increase in peptide YY and ghrelin, a decreased cholecystokinin response, and lower fasting levels of leptin.[53] The sleeve is removed by endoscopy after 12 months.

The gastro-duodeno-jejunal bypass sleeve (GJBS or EndoBypass System; ValenTx, Inc. Carpinteria, CA, USA) is a 120-cm device, attached at the level of the esophago-gastric junction. The sleeve is placed and removed endoscopically after 12 months. It tries to mimic the gastric restriction, and the proximal jejunal bypass of a standard Roux-en-Y gastric bypass.

Thermal ablation of the superficial duodenal mucosa using radiofrequency is the main principle of the Revita duodenal mucosal resurfacing procedures (Fractyl Laboratories, Cambridge, MA, USA). The idea of this endoscopic technique is to alter the enteroendocrine signaling in the duodenum, which can ameliorate type 2 diabetes control.

Self-Assembling MagnetS for ENdoscopy (SAMSEN, GI windows, Boston, MA, USA) is a procedure in which magnets are placed at the level of the endoscopically created gastrojejunostomy, thus enabling in the future and endoscopic single-anastomosis gastric bypass, without the exact measurement of the bypassed small bowel limb.

Results

The EndoBarrier procedure is well documented in different randomized controlled trials, often set up as a presurgical weight loss intervention in comparison with diet. All studies report on significantly better weight loss results, with 22% EWL after 3 months, 32.0% EWL after 6 months, and 47.0% EWL after 12 months compared to control subjects,[54-56] and statistically significant improvements in blood pressure, hemoglobin A1c, and choles-

terol. A varying amount of patients, between 13 and 38% of the investigated groups, required premature explantation of the device due to bleeding, migration, obstruction, pain, and anchor dislocation.[57, 58] Note that as of March 2015, the EndoBarrier trials were placed on hold by the FDA in the USA due to 4 cases of bacterial infection of the liver out of 325 enrolled study subjects.

The GJBS was studied in 12 patients, of which 2 underwent explantation of the device in the first month due to intolerance, and 4 others had partial cuff detachment and uncomplete therapeutic effect.[59] In 6 patients the % EWL after one year was 54%, and 14 months after explantation the % EWL remained 30%. In all 10 patients, the device was well tolerated for one year.

The Revita procedure and the SAMSEN technique are still in an early phase of investigation.

Conclusions

Worldwide, the problem of obesity has risen towards epidemic proportions, affecting in large parts of the world more than 35% of the population.[4] Besides prevention of developing overweight, the treatment of obesity as a chronic disease and its associated comorbidities is of the utmost importance to add quality-adjusted life years in our population, and decrease the impact on the costs for health care systems all over the world. Bariatric surgery can be considered as a clinically effective and cost-effective intervention for the treatment of the moderately to severely obese patient in comparison to conservative measures.[59, 60] Risk and cost benefit analysis suggest that surgical guidelines should even be reconsidered, with redefining the threshold for bariatric surgery to a BMI of 35 instead of 40 kg/m^2 and a BMI of 30 instead of 35 kg/m^2 with comorbidities.[61] Despite the few available randomized controlled trials in the field of bariatric surgery, systematic reviews show favorable outcomes after laparoscopic gastric bypass and sleeve gastrectomy in terms of weight loss results, resolution of comorbidities and risk of complications compared to other weight reduction measures.[62, 63] In sleeve gastrectomy patients, mean % EWL at 5, and 8 years was reported to be 61%, and 52%, respectively, with low risks of short- and long term complications.[64] In gastric bypass patients, mean % EWL was 60% at 7 years, with >50% resolution of comorbidities.[65]

A considerable amount of patients will not apply for surgery, for various reasons mentioned in the introduction section. The role of the endoscopist in adding therapeutic strategies in the armentarium of the battle against obesity remains unclear. Our review aimed to gather evidence concerning the most valuable innovations in this field. Endoscopic bariatric interventions can provide minimally invasive treatment approaches for both primary and non-primary bridge obesity therapy. Although the idea of not undergoing a surgical intervention might be tempting for many patients, we have to temper our enthusiasm until added value is proven. In this regard, further studies are needed concerning long term % EWL results and complication rates, resolution of comorbidities, reproducibility of the technique and randomized controlled trials revealing which patient group might benefit from conservative, endoscopic or surgical therapy. We have to take into account that endoscopic techniques are often more complex than primary bariatric surgery, with obese patients under general anesthesia undergoing specialized, heroic interventions with mean procedure times up to 123-142 minutes when gastroplasties or plications are performed.[30, 34, 38]

Currently, evidence is available for Orbera intragastric balloon use in primary and nonprimary bridge obesity patient groups, leading to 25% EWL one year after implantation.[10] Promising results are reported using the duodeno-jejunal bypass liner, leading to 35% EWL at 12 months, but randomized controlled studies should report on further data. Serious adverse events were described [18, 57, 58] and due to liver abscesses the EndoBarrier trials were placed on hold by the FDA in the USA. Nevertheless, the American Society for Gastrointestinal Endoscopy consider the

Orbera balloon and the EndoBarrier therapy as safe.[10] Despite all published small series, there is currently no evidence for adopting other transoral bariatric devices in the routine clinical practice.

Vagal nerve stimulation proved to be an interesting intervention in the ReCharge trial,[48-50] with a % EWL of 25.8% after 12 months, of 24.4% after 15 months, of 23.5% after 18 months, and of 22% after 24 months of vBloc therapy.

In terms of % EWL and remission of comorbidities in the obese subject, no new device currently reviewed could compete with the effect of safe and well-documented bariatric interventions, such as laparoscopic Roux-en-Y gastric bypass or sleeve gastrectomy, but defining the role of different therapeutic approaches and innovations is an interesting field of research in the near future.

References

1. Berrington de Gonzalez A, Hartge P, Cerhan JR, Flint AJ, Hannan L, MacInnis RJ, *et al.* Body-mass index and mortality among 1.46 million white adults. N Engl J Med 2010;363:2211-9.
2. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brody J, *et al.* A potential decline in life expectancy in the United States in the 21st century. N Engl J Med 2005;352:1138-45.
3. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i-xii. 1-253.
4. The GBD 2013 Obesity Collaboration. Global, regional and national prevalence of overweight and obesity in children and adults 1980-2013: a systematic analysis. Lancet;384:766-81.
5. Follow-up to the political declaration of the high-level meeting of the general assembly on the prevention and control of non-communicable diseases;Geneva, Switzerland: World Health Assembly;2013.
6. Sjostrom L. Review of the key results from the Swedish Obese Subjects (SOS) trial – A prospective controlled intervention study of bariatric surgery. J Intern Med 2013;273:219-34.
7. Buchwald H, Oien DM. Metabolic/bariatric surgery worldwide 2011. Obes Surg 2013;23:427-36.
8. Phillips RJ, Powley TL. Gastric volume rather than nutrient content inhibits food intake. Am J Physiol 1996;271:R766-9.
9. Hogan RB, Johnston JH, Long BW, Sones JQ, Hinton LA, Bunge J, *et al.* A double-blind, randomized sham-controlled trial of the gastric bubble for obesity. Gastrointest Endosc 1989;35:381-5.
10. Abu Dayyeh BK, Kumar N, Edmundowicz SA, Jonnalagadda S, Larsen M, Sullivan S, *et al.* ASGE bariatric endoscopy task force systematic review and meta-analysis assessing the ASGE PIVI tresholds for adopting endoscopic bariatric therapies. Gastrointestinal Endosc 2015;82:425-38.
11. Busetto L, Enzi G, Inelmen EM, Costa G, Negrin V, Sergi G, Vianello A. Obstructive sleep apnea syndrome in morbid obesity: effects of intragastric balloon. Chest 2005;128:618-23.
12. Crea N, Pata G, Della Casa D, Minelli L, Maifredi G, Di Betta E, Mittempergher F. Improvement of metabolic syndrome following intragastric balloon: 1 year follow-up analysis. Obes Surg 2009;19:1084-8.
13. Lee YM, Low HC, lim LG, Dan YY, Aung MO, Cheng CL, *et al.* Intragastric balloon significantly improves nonalcoholic steatohepatitis: a pilot study. Gastrointest Endosc 2012;76:756-60.
14. Genco A, Lopez-Nava G, Wahlen C, Maselli R, Cipriano M, Sanchez MM, *et al.* Multi-center European experience with intragastric balloon in overweight populations: 13 years of experience. Obes Surg 2013;23:515-21.
15. Busseto L, Segato G, De Luca M, Bortolozzi E, MacCari T, Magon A, *et al.* Preoperative weight loss by intragastric balloon in super-obese patients treated with laparoscopic gastric banding: a case-control study. Obes Surg 2004;14:671-6.
16. Zerrweck C, Maunoury V, Calazzo R, Branche J, Dezfoulian G, Bulois P, *et al.* Preoperative weight loss with intragastric balloon decreases the risk of significant adverse outcomes of laparoscopic gastric bypass in super-obese patients. Obes Surg 2012;22:777-82.
17. Leeman MF, Ward C, Duxbury M, de Beaux AC, Tulloh B. The intragastric balloon for preoperative weight loss in bariatric surgery: is it worthwile? Obes Surg 2013;23:1262-5.
18. Abu Dayyeh BK, Edmundowicz SA, Jonnalagadda S, Larsen M, Sullivan S, Thompson CC, Banerjee S. Endoscopic bariatric therapies. Gastrointest Endosc 2015;81:1073-86.
19. Caglar E, Dobrucali A, Bal K. Gastric balloon to treat obesity: filled with air or fluid? Dig Endosc 2013;25:502-507.
20. Ponce J, Woodman G, Swain J, Wilson E, English W, Ikramuddin S, *et al.* The REDUCE pivotal trial: a prospective, randomized controlled pivotal trial of a dual intragastric balloon for the treatment of obesity. Surg Obes Relat Dis 2015;11:874-81.
21. Machytka E, Klvana P, Kornbluth A, Peikin S, Mathus-Vliegen LE, Gostout C, *et al.* Adjustable intragastric balloons: a 12-month pilot trial in endoscopic weight loss management. Obes Surg 2011;21:1499-507.
22. Brooks J, Srivastava ED, Mathus-Vliegen EMH. One-year adjustable intragastric balloons: results in 73 consecutive patients in the UK. Obes Surg 2014;24:813-9.
23. Marinos G, Eliades C, Raman MV, Greenway F. Weight loss and improved quality of life with a nonsurgical endoscopic treatment for obesity: clinical results from a 3- and 6-month study. Surg Obes Relat Dis 2014;10:929-34.
24. Sauer N, Rösch T, Pezold J, Reining F, Anders M, Groth S, *et al.* A new endoscopically implantable device (SatiSphere) for treatment of obesity – efficacy, safety, and metabolic effects on glucose, insulin, and GLP-1 levels. Obes Surg 2013;23:1727-33.
25. Lopez-Nava G, Galvao MP, da Bautista-Castano I, Jimenez A, De Grado T, Fernandez-Corbelle JP. Endoscopic sleeve gastroplasty for the treatment of obesity. Endoscopy 2015;47:449-52.
26. Sharaiha RZ, Kedia P, Kumta N, DeFilippis EM, Gaidhane M, Shukla A, *et al.* Initial experience with endoscopic sleeve gastroplasty: technical success and reproducibility in the bariatric population. Endoscopy 2015;47:164-6.
27. Abu Dayyeh BK, Acosta Cardenas AJ, Camilleri M,

Mundi MS, Rajan E, Topazian MD, *et al.* Endoscopic sleeve gastroplasty alters gastric physiology and induces loss of body weight in obese individuals. Clin Gastroenterol Hepatol 2015. pii: S1542-3565(15)01714-0.
28. Fogel R, De Fogel J, Bonilla Y, De La Fuente R. Clinical experience of transoral suturing for an endoluminal vertical gastroplasty: 1-year follow-up in 64 patients. Gastrointest Endosc 2008;68:51-8.
29. Fogel R, De Fogel J. Transoral vertical gastroplasty as a viable treatment for childhood obesity - a study of 21 adolescents with up to 18 months of follow-up. Gastrointest Endosc 2009;69:AB169-AB170.
30. Brethauser SA, Chand B, Shauer PR, Thompson CC. Transoral gastric volume reduction as intervention for weight management: 12-month follow-up of TRIM trial. Surg Obes Relat Dis 2012;8:296-303.
31. Devière j, Ojeda Valdes G, Cuevas Herrera L, Closset J, Le Moine O, Eisendrath P, *et al.* Safety, feasibility and weight loss after transoral gastroplasy: first human multicenter study. Surg Endosc 2008;40:406-13.
32. Familiari P, Costamagna G, Bléro D, Le Moine O, Perri V, Boskoski I, *et al.* Transoral gastroplasty for morbid obesity: a multicenter trial with a one-year outcome. Gastrointest Endosc 2011;74:1248-58.
33. Nanni G, Familiari P, Mor A, Iaconelli A, Perri V, Rubino F, *et al.* Effectiveness of the Transoral Endoscopic Vertical Gastroplasty (TOGa): a good balance between weight loss and complications, if compared with gastric bypass and biliopancreatic diversion. Obes Surg 2012;22:1897-902.
34. Verlaan T, Paulus GF, Mathus-Vliegen EM, Veldhuyzen EA, Conchillo JM, Bouvy ND, *et al.* Endoscopic gastric volume reduction with a novel articulating plication device is as safe and effective in the treatment of obesity (with video). Gastrointest Endosc 2015;81:312-320.
35. Espinos JC, Turro R, Mata A, Cruz M, da Costa M, Villa V, *et al.* Early experience with the Incisionless Operating Platform (IOP) for the treatment of obesity: the primary obesity surgery endolumenal (POSE) procedure. Obes Surg 2013;23:1375-83.
36. Lopez-Nava G, Bautista-Castano I, Jimenez A, de Grado T, Fernandez-Corbelle JP. The Primary Obesity Surgery Endolumenal (POSE) procedure: one-year patient weight loss and safety outcomes. Surg Obes Relat Dis 2015;11:861-5.
37. Espinos JC, Turro R, Moragas G, Bronstone A, Buchwald JN, Mearin F, *et al.* Gastrointestinal physiological changes and their relationship to weight loss following the POSE procedure. Obes Surg 2015 [Epub ahead of print].
38. de Jong K, Mathus-Vliegen EM, Veldhuyzen EA, Eshuis JH, Fockens P. Short-term safety and efficacy of the Trans-Oral Endoscopic Restrictive Implant System for the treatment of obesity. Gastrointest Endosc 2010;72:497-504.
39. Thompson CC, Chand B, Chen YK, Abu Dayyeh BK, Lautz DB, Thompson CC. Endoscopic suturing devices for transoral outlet reduction in patients with weight regain following Roux-en-Y gastric bypass. Endoscopy 2013;145:129-37.
40. Kumar N, Thompson CC. Comparison of a superficial suturing device with a full-thickness suturing device for transoral outlet reduction (with videos). Gastrointest Endosc 2014;79:984-9.
41. Kumar N, Thompson CC. Transoral outlet reduction for weight regain after gastric bypass: long-term follow-up. Gastrointest Endosc 2015. pii: S0016-5107(15)02811-4.
42. Horgan S, Jacobsen G, Weiss GD, Oldham JS Jr, Denk PM, Borao F, *et al.* Incisionless revision of post-Roux-en-Y bypass stomal and pouch dilation: multicenter registry results. Surg Obes Relat Dis 2010;6:290-5.
43. Goyal V, Holover S, Garber S. Gastric pouch reduction using StomaphyX in post Roux-en-Y gastric bypass patients does not result in sustained weight loss: a retrospective analysis. Surg Endosc 2013;27:3417-20.
44. Mikami D, Needleman B, Narula V, Durant J, Melvin WS. Natural orifice surgery: initial US experience utilizing the StomaphyX device to reduce gastric pouches after Roux-en-Y gastric bypass. Surg Endosc 2010;24:223-8.
45. Eid GM, McCloskey CA, Eagleton JK, Lee LB, Courcoulas AP. StomaphyX vs a sham procedure for revisional surgery to reduce regained weight in Roux-en-Y gastric bypass patients: a randomized clinical trial. JAMA Surg 2014;149:372-9.
46. Bolton J, Gill RS, Al-Jahdali A, Byrns S, Shi X, Birch DW, Karmali S. Endoscopic revision (StomaphyX) versus formal surgical revision (gastric bypass) for failed vertical banded gastroplasty. J Obes 2013;2013:108507.
47. Sarr MG, Billington CJ, Brancatisano R, Brancatisano A, Toouli J, Kow L, *et al.* The EMPOWER study: randomized, prospective, double-blind, multicenter trial of vagal blockade to induce weight loss in morbid obesity. Obes Surg 2012;22:1771-82.
48. Ikramuddin S, Blackstone RP, Brancatisano A, Toouli J, Shah SN, Wolfe BM, *et al.* Effect of reversible intermittent intra-abdominal vagal nerve blockade on morbid obesity: the ReCharge randomized clinical trial. JAMA 2014;312:915-22.
49. Shikora SA, Wolfe BM, Apovian CM, Anvari M, Sarwer DB, Gibbons RD, *et al.* Sustained Weight Loss with Vagal Nerve Blockade but Not with Sham: 18-Month Results of the ReCharge Trial. J Obes 2015;2015:365604.
50. Shikora SA, Toouli J, Herrera MF, Kulseng B, Brancatisano R, Kow L, *et al.* Intermittent Vagal Nerve Block for Improvements in Obesity, Cardiovascular Risk Factors, and Glycemic Control in Patients with Type 2 Diabetes Mellitus: 2-Year Results of the VBLOC DM2 Study. Obes Surg 2015 [Epub ahead of print].
51. Sullivan S, Stein R, Jonnalagadda S, Mullady D, Edmundowicz S. Aspiration therapy leads to weight loss in obese subjects: a pilot study. Gastroenterology 2013;145:1245-52.
52. Forssell H, Norén E. A novel endoscopic weight loss therapy using gastric aspiration: results after 6 months. Endoscopy 2015;47:68-71.
53. de Jonge C, Rensen SS, Verdam FJ, Vincent RP, Bloom SR, Buurman WA, *et al.* Impact of duodenal-jejunal exclusion on satiety hormones. Obes Surg 2015 [Epub ahead of print].
54. Tarnoff M, Rodriguez L, Escalona A, Ramos A, Neto M, Alamo M, *et al.* Open label, prospective, randomized controlled trial of an endoscopic duodenal-jejunal bypass sleeve versus low calorie diet for preoperative weight loss in bariatric surgery. Surg Endosc 2009;23:650-6.
55. Koehestanie P, de Jonge C, Berends FJ, Janssen IM, Bouvy ND, Greve JW. The effect of the endoscopic duodenal-jejunal bypass liner on obesity and type 2 diabetes mellitus, a multicenter randomized controlled trial. Ann Surg 2014;260:984-92.
56. Escalona A, Pimentel F, Sharp A, Becerra P, Slako M, Turiel D, *et al.* Weight loss and metabolic improvements in morbidly obese subjects implanted for 1 year with an endoscopic duodenal-jejunal bypass liner. Ann Surg 2012;255:1080-5.
57. Schouten R, Rijs CS, Bouvy ND, Hameeteman W, Koek GH, Janssen IM, *et al.* A multicenter, randomized efficacy study of the EndoBarrier Gastrointestinal Liner for presurgical weight loss prior to bariatrical surgery. Ann Surg 2010;251:236-243.
58. Gersin KS, Rothstein RI, Rosenthal RJ, Stefanidis D,

Deal SE, Kuwada TS, *et al.* Open-label, sham-controlled trial of an endoscopic duodenojejunal bypass liner for preoperative weight loss in bariatric surgery candidates. Gastrointest Endosc 2010;71:976-82.
59. Picot J, Jones J, Colquitt JL, Loveman E, Clegg AJ. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. Health Techn Assess 2009;13:1-190, 215-357
60. Warren JA, Ewing JA, Hale AL, Blackhurst DW, Bour ES, Scott JD. Cost-effectiveness of Bariatric Surgery: Increasing the Economic Viability of the Most Effective Treatment for Type II Diabetes Mellitus. Am Surg 2015;81:807-11.
61. Sinha AC, Singh PM, Bhat S. Are we operating too late? Mortality Analysis and Stochastic Simulation of Costs Associated with Bariatric Surgery: Reconsidering the BMI Threshold. Obes Surg 2015 [Epub ahead of print].
62. Colquitt JL, Pickett K, Loveman E, Frampton GK. Surgery for weight loss in adults. Cochrane Database Syst Rev 2014;8:CD003641.
63. Puzziferri N, Roshek TB, Mayo HG, Gallagher R, Belle SH, Livingston EH. Long-term follow-up after bariatric surgery: a systematic review. JAMA 2014;312:934-42.
64. Alvarenga ES, Lo Menzo E, Szomstein S, Rosenthal RJ. Safety and efficacy of 1020 consecutive laparoscopic sleeve gastrectomies performed as a primary treatment modality for morbid obesity. A single-center experience from the metabolic and bariatric surgical accreditation quality and improvement program. Surg Endosc 2015 [Epub ahead of print].
65. Dogan K, Betzel B, Homan J, Aarts EO, Ploeger N, de Boer H, *et al.* Long-term effects of laparoscopic Roux-en-Y gastric bypass on diabetes mellitus, hypertension and dyslipidaemia in morbidly obese patients. Obes Surg 2014;24:1835-42.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Article first published online: February 29, 2016.