**What is the role of bariatric surgery in the management of obesity?**

E Panteliou, A D Miras

Section of Investigative Medicine, Division of Diabetes, Endocrinology & Metabolism, Imperial College London, 6th floor Commonwealth Building, Hammersmith Hospital, Du Cane Road, London, W12 0NN, UK. 02033134843, eleftheria@doctors.org.uk.

**Abstract**

Diet,exercise, cognitive behavioural therapy and pharmacotherapy are some of the means assisting patients to lose weight, with bariatric surgery being the most effective. Over the last two decades the increased awareness of the systemic benefits of bariatric surgery as well as the improved safety and the wider use of the laparoscopic approach has made bariatric surgery flourish. In the United Kingdom (UK), the adjustable gastric band (AGB) (10%), vertical sleeve gastrectomy (VSG) (37%) and Roux-en-Y Gastric Bypass (RYGB) (45%) are the three commonest procedures. Obesity associated mortality and co-morbidities such as Type 2 Diabetes, hypertension, dyslipidaemia, obstructive sleep apnoea, renal dysfunction and depression improve significantly with bariatric surgery. The mechanisms of weight loss extend beyond restriction and malabsorption and include changes in hunger and satiety, food preferences, and possibly energy expenditure. Despite its safety and efficacy, bariatric surgery is underutilised as less than 1% of adults with obesity receive it. In view of the evolution of obesity into a global threat access to bariatric surgery should be increased, whilst developing safer and less invasive weight loss treatments

**Keywords:** Obesity, bariatric surgery, metabolic surgery, diabetes, gut hormones.

**Introduction**

Obesity is a fast spreading metabolic disease of pandemic proportions. Within the last 30 years, its prevalence has increased from 7% to 25% with severe obesity (BMI>40kg/m2) affecting 2.4% of the population1. If the current trendcontinues, by 2030 overweight and obese individuals will consist 60% of the world’s population2. The obesity epidemic is a result of complex interactions between genetics, epigenetics, cultural and environmental parameters3. In 2010, 3.4 million deaths and 4% of disability-adjusted life years (DALYs) were attributed to obesity4. Obesity in adults can be defined as a Body Mass Index (BMI) of ≥30kg/m2 and overweight as BMI of 25-29.9kg/m2. For some ethnic groups lower BMI cut-off points should be adopted5.

**Non-surgical treatment options for obesity**

Most treatments targeting obesity such as diet, exercise, cognitive behavioural therapy and pharmacotherapy are less effective compared to obesity surgery that can achieve more significant and sustainable weight loss.

Diet

A 15–30% reduction in caloric intake can lead to weight loss and generally a daily deficit of 600kcal can achieve 0.5kg weight loss per week. There are 2 main types of conventional diets: the balanced, low-calorie (800-1200kcal/day) diets or reduced portion size diets and the diets that emphasize on a particular macronutrient (>1200 kcal/day). Although, the former type is the most commonly recommended by health care professionals, it does not achieve sustained weight loss. Interestingly, obese patients are less likely to lose weight on diet compared to individuals who have never been obese, requiring the daily consumption of 10-15% less calories in order to maintain a normal body weight6.

Exercise

Physical activity is associated with a number of positive effects such as decreased intra-abdominal adiposity, increased free fat mass, increased resting energy expenditure, reduced blood pressure, improved insulin sensitivity, dyslipidaemia and wellbeing. Lifestyle modifications result in a 5-10% weight loss commonly regained within 1-2 years. In the Look AHEAD (Action for Health in Diabetes) study, examining the effect of intense lifestyle interventions (1200-1800kcal daily and 175minutes of moderate physical activity weekly) in patients with type 2 diabetes (T2DM), 34.5% in the intervention group lost at least 10% of their weight in the first year that was maintained in 42.2% 4 years later7, manifesting the difficulty in achieving and maintaining even a moderate degree of weight loss despite the intensity and long duration of the programme.

Pharmacotherapy

The use of anti-obesity medications is recommended by the Endocrine Society (2015) in patients with a BMI≥30kg/m2 or ≥27kg/m2 in the presence of obesity-related complications. The target weight loss, in the first three months of use, is ≥5% in non-diabetes and ≥3% in diabetes patients. A limited number of medications are currently licensed with a variety of mechanisms of action that include reduced fat absorption, centrally acting appetite suppressants such as serotonin type-2C and norepinephrine agonists and gut hormone agonists such as glucagon-like-peptide 1 (GLP-1) agonists. Weight loss with obesity drugs ranges between 4-11% and is maintained as long as the medication is continued8.

**Obesity Surgery**

Obesity surgery is the most effective way of long-lasting weight loss especially for the morbidly obese9. The early classification of obesity surgery into restrictive or malabsorptive fails to describe the complex functional alteration of the gastrointestinal tract as a result of the anatomical rearrangement10. Changes in gut hormones, as well as the associated caloric reduction are only some of the mechanisms explaining the weight loss and associated metabolic benefits of obesity surgery11. The recognition of its positive systemic effects and improved safety has lead into an increase in the total number of obesity procedures worldwide over the last two decades, with 468,609 obesity procedures performed in 2013, one third of which in the United States (US)/Canada.

Factors that determine the choice of obesity surgery

There are no algorithms assisting with the decision of choosing the most suitable obesity surgery procedure. Parameters such as degree of obesity, metabolic comorbidities, target outcomes in terms of weight loss and improvement of associated conditions, risks of the procedure and patient needs and concerns should all be taken into consideration. A multidisciplinary approach should be adopted in balancing out benefits and risks. Laparoscopic Adjustable Gastric Band (LAGB) tends to be recommended for patients with BMI of 30-40kg/m2 who have no significant comorbidities, prefer a reversible procedure and will reliably attend the required follow-up period12. Roux-en-Y gastric bypass (RYGB) is technically more demanding and its safety and efficacy have been established over a number of years, exhibiting a number of positive metabolic effects especially with T2DM. Vertical Sleeve Gastrectomy (VSG) is a non-reversible procedure with weight loss and metabolic results comparable to RYGB. Biliopancreatic Diversion (BPD) is generally reserved for the extremely obese (BMI>50kg/m²) and leads into the most significant weight loss of all obesity procedures and remission of metabolic disturbances12.

Popularity of obesity procedures

In the UK, RYGB is the commonest performed procedure at 45%, followed by VSG at 37% and LAGB at 10%13. The number of National Health Service (NHS)-funded obesity surgery has increased 14-folds between 2003/04 and 2009/10. In more detail, LAGB was the most commonly performed obesity procedure worldwide between 2008 and 2010. The poor long-term results and the high reoperation rates secondary to complications such as pouch dilatation, dysphagia and erosion has progressively made it less favourable14. Contrary to that, the popularity of VSG has increased as a result of its significant and long-lasting weight loss.

Eligibility criteria

Surgical candidates should have BMI of ≥40.0kg/m2 or 35-39.9kg/m2 with weight-related co-morbidities expected to improve with surgery as outlined by guidelines used in the UK, Europe and the US. Individuals with BMI≥50kg/m2 qualify for surgery as a first line treatment and patients with T2DM and BMI of 30-34.9kg/m2 might be suitable for metabolic surgery after individual consideration15,16. According to the IFSO-APC (International Federation For The Surgery Of Obesity And Metabolic Disorders Asia Pacific Chapter) consensus statement in 2011, obesity surgery should be considered for candidates with BMI>35kg/m2 regardless of comorbidities and BMI>30kg/m2 for patients with T2DM and metabolic syndrome who are inadequately controlled. Asian candidates with BMI>27.5kg/m2 might be also considered if judged suitable17.

Anatomical changes

In LAGB, a silicone band around the upper part of the stomach creates a small pouch restricting food consumption and suppressing hunger via vagal afferent signals. The outlet diameter is adjustable and the procedure reversible. The mean total body weight loss (TWL) at 1 year is 15.8%18. In RYGB a 15-30mls pouch created from the upper part of the stomach is anastomosed to the jejunum, leaving an alimentary limb of 100–150cm, which meets a 50cm biliopancreatic limb (BPL) where food and digestive enzymes mix. RYGB is irreversible and nutritional deficiencies require lifelong replacement. In RYGB TWL is 30.0±8.5% at 1 year post-surgery19. In VSG the size of the stomach is decreased by 75% by removing the entire fundus and the majority of the body. Although initially developed as a first-stage operation prior to Biliopancreatic Diversion (BPD) with Duodenal Switch (DS) for high-risk patients it was soon realised that only 6% of patients required further surgery20. VSG is very effective and safe and has a TWL of 28.9% 1 year after surgery21. In BPD a gastric pouch greater than the one in RYBG is created by removing the distal part of the stomach. The small bowel is transacted halfway between the ligament of Treitz and the ileocaecal valve with one end anastomosed to the gastric pouch creating the alimentary track and the other end (BPL) joining the alimentary 50 cm before the ileocaecal valve22. In the DS version, a vertical sleeve gastrectomy is created and the alimentary track consists of a duodenoenterostomy which meets the BPL more than 100cms before the ileocaecal valve. It is generally reserved for the superobese (BMI>50kg/m2) with proven benefit in achieving and maintaining better weight loss results and leading to greater patient satisfaction as the tolerated meals are larger compared to other procedures. BPD results in a mean TWL of 57kg and carries a higher rate of mortality and long term nutritional deficiencies, representing only 2% of total worldwide obesity surgery procedures19,23. The BMI achieved in BPD and RYGB patients is still in the overweight range (28-30kg/m2) and takes 2 years postoperatively to stabilize with some weight regain after that24.

**Benefits of obesity surgery**

Effects of obesity surgery on weight loss and diabetes versus non-surgical treatments

In a meta-analysis of 11 Randomised Controlled Trials (RCTs) on the effects on weight loss and comorbidities of various obesity procedures versus medical treatment, the 1-2 year weight loss was greater by 26kg in the obesity group with a relative risk reduction for T2DM of 22.1-5.3 depending on whether the calculation were based on complete case analysis or a conservative risk calculation15,16,25,26,27,28. In the Swedish Obese Study (SOS), the mean total body weight loss of surgical patients at 2, 10, 15, and 20 years was −23%, −17%, −16%, and −18% in the surgical group compared with 0%, 1%, −1%, and −1% in the control group, while T2DM remission was 72% at 2 years and 36% at 10 years. An observational study performed in Utah comparing patients 7 years post-RYGB and controls showed reduction in all-cause mortality by 40%, cardiovascular death by 49% and T2DM related death by 92%29. The prospective Utah Obesity Study that compared patients who had RYGB with obesity surgery seekers who had no surgery and obese individuals showed that the weight loss in the first group was 27.7%, compared with 0.2% weight gain in the second group and no weight change in the last group at six years30. Diabetes remission data at the same study, showed remission in 62% of RYGB patients compared with 8% and 6% at the other two groups31.

Observational studies have shown that obesity surgery can prevent the progression of impaired glucose tolerance in almost all cases and resolve pre-existing T2DM in 64–93% an outcome readjusted to 41% when the 2009 consensus criteria of diabetes remission are applied32,33. These results are maintained 5 and 10 years post-operatively34,35. In the obese patients with a longer history of T2DM or on insulin pre-operatively, rates of remission are 70% and 50%, respectively36,37. Choosing the right patient is critical for obesity surgery to be successful in terms of diabetes resolution. Less than 30% of overweight or mildly obese patients with T2DM maintain their improved diabetes control long-term as a result of weight regain38,39. It seems that the reduced insulin resistance is solely responsible for the observed benefit in the mildly obese whereas in morbidly obese diabetic subjects, the compensatory increased beta cell mass is also contributing40.

Improvement in other comorbidities and mortality

Post laparoscopic RYGB complete resolution of hypertension was observed in 46% of patients and improvement in 19%16,41. A reduction in the need for antihypertensive agents was seenand hypertension of shorter duration was associated with better results. In LAGB patients, hypertension relapsed after 6–8 years of follow up in the SOS study42.

Following RYGB low-density lipoprotein cholesterol (LDL) was decreased by 31%, high-density lipoprotein (HDL) increased by 39% and triglyceride levels decreased by 63% ) at 12 months with 82% of patients no longer requiring lipid lowering medications43. Obesity surgery results in resolution of Obstructive Sleep Apnoea (OSA) in 86% of patients and improvement in 9%44,45. A meta-analysis by Mummadi *et al* reported an improvement of steatosis, steatohepatitis and fibrosis of the liver after obesity surgery at 91.6%, 81.3% and 65.5% respectively46. In the SOS study of over 4000 obese patients, depression and anxiety in the year after surgery compared to obese controls was significantly decreased47. There is some evidence that obesity surgery also improves mental function and leads to a decreased incidence of fatal and non-fatal cancers in women48. Mortality reduction due to coronary heart disease, T2DM and cancer is reduced by 56%, 92%, and 60% respectively49,50.

Effects of surgery during the menopause

In a study by Sugerman *et al* patients, the majority of who had an open RYGB, were divided into an over and under 60 years of age groups. The characteristics in terms of gender (78% female), ethnic group (85% white) and mean BMI (44.9±7.4kg/m2) were similar. The older group had a smaller degree of excess weight loss (57% EWL) compared with the younger one (65% EWL) at one year. Weight maintenance at five years was also smaller (49% EWL) compared with the younger group (59% EWL)51. BMI reduction (from 44 to 36kg/m2) was also less significant in LAGB patients over the age of 60 compared with the younger group (from 45 to 30 kg/m2)52. Perry *et al* showed that comorbidities were reduced in patients over the age of 65 receiving obesity surgery compared with patients of the same age group solely receiving medical therapy for obesity53. Improvement in other areas including physical and mental function, work capacity, confidence, sexual activity and health-related quality of life was also observed in older patients receiving surgery54,55. In a study by Ochner *et al*, two different age groups of women (20-45 and 55-65 years old), respectively presumed to be pre and post-menopausal, were compared at 12 and 24 months post-RYGB and LABG. EBWL was 10% less in the post-menopausal women following LABG (P<0.01), although no difference was observed between age groups in patients undergoing RYGB56.

**Complications of obesity surgery**

Obesity surgery is generally safe, with a 30-day mortality of 0.2% for laparoscopic RYGB and VSG, 0.1% for LAGB and 0.8% for BPD. A number of factors such as the type of surgery, the use of laparoscopic techniques, the patient’s pre-operative functional status and comorbidities and the surgical experience of the centre can influence the outcomes in terms of peri-operative morbidity and mortality. The immediate surgical complications include anastomotic leaks (0.8-6%), bleeding (0.4-4%), wound infection (0.3-9%) and venous thromboembolism (0.3-2.1%), while chronic diarrhoea (up to 55% of patients with RYBG and BPD), bowel obstruction, strictures and gallstones (up to 50% post-RYGB) consist longer term surgical complications. The main medical complications associated with obesity surgery are nutritional deficiencies such as iron (12-47%), vitamin B12 (4%), thiamine (18%) and zinc (36-51%) deficiency, osteoporosis, dumping syndrome (up to 50% post RYGB) and post-prandial hypoglycaemia. The SOS study, involving more than 4000 patients, showed improvement in depression and anxiety one year later in obese patients undergoing obesity surgery compared to controls that only received lifestyle modifications46. Interestingly, the risk of suicide and addictive behaviour increased after bariatric surgery57,58,59.

**Cost of obesity surgery**

In the US, treating obesity and the associated comorbidities takes up to 16.5% of the total health care expenses60(168 billion dollars/year). In the UK, overweight and obesity cost the NHS £4.2 billion in 2007 with projected direct costs of 8.3 billion/year (12% of NHS budget) and indirect costs exceeding £37 billion/year by 202561. The estimated direct cost of obesity in the European Union is 2.6% of total costs in health care and worldwide up to 7%62. In financial terms, the benefits of obesity surgery are more substantial in the long term63,64 and for patients with T2DM65,66. Although obesity surgery is known to be an impressive obesity treatment, the financial benefits for health care systems are not clearly demonstrated. The SOS study that followed-up obesity patients (68% of whom had vertical banded gastroplasty) for 20 years, showed that in the first 6 years after surgery outpatient and inpatient costs were higher for obesity patients compared to controls, something that equalised between the groups in the following years while the prescription costs were lower for the surgical group at the studied period (7-20 years)67. Sussenbach *et al*, found that the annual healthcare costs decreased almost 4-fold in the three years following RYGB contrary to a study by Maciejewski *et al* describing higher costs at 3 years68,69. Weiner *et al*, found similar costs in the 6 follow-up period post-surgery, when 30,000 obesity surgical patients were compared with matched controls70.

**Conclusion**

The prevention of obesity remains the main objective in managing this epidemic and its devastating consequences. The importance of obesity surgery extends, beyond its obvious weight reducing purpose, into achieving a better understanding of this complex disease and assisting us develop more individualised treatments. Obesity surgery has been transformed over the last 20 years with the introduction of laparoscopic techniques. Its multiple benefits are well established with studies demonstrating the reduction in mortality and morbidity associated with obesity. Despite its safety and efficacy, obesity surgery is underutilised as less than 1% of adults with morbid obesity receive it. This is a result of limited financial resources in healthcare, lack of initiative from medical practitioners to refer patients appropriately and reluctance of suitable patients to have surgery. In view of the obesity’s evolution into a major global threat access to obesity surgery should be improved, develop safer and less invasive techniques and offer more non-surgical treatments. The nature of obesity surgery is anticipated to change in view of our better understanding of the neural and hormonal pathways involved and anatomical manipulation will be individualized depending on the desired outcome.

Our understanding of the mechanisms underlying the positive effects of obesity surgery can accelerate the development of non-surgical treatments with similar metabolic results. GLP-1, peptide tyrosine tyrosine (PYY) and oxyntomodulin, gut hormones involved in the post obesity changes are attractive pharmacological targets for obesity. Endoluminal bypass devices, such as the duodenojejunal bypass liner, have also developed as a result of our increasing knowledge of the role of the gut in weight regulation.

**References**

1. Stegenga H, Haines A, Jones K, Wilding J. Identification, assessment, and management of overweight and obesity: summary of updated NICE guidance. BMJ 2014;349:g6608.
2. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. Int J Obes (Lond) 2008;32:1431–1437.
3. Farooqi S, O’Rahilly S. Genetics of obesity in humans. Endocr Rev 2006;27:710–718.
4. Ng M, Fleming T, Robinson M, *et al*. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384:766–781.
5. James WP. The epidemiology of obesity: the size of the problem. J Intern Med 2008; 263: 336–352.
6. Leibel R, Rosenbaum M, Hirsch J. Changes in energy expenditure. N Engl J Med 1995;332:621-628.
7. Wadden TA, Bantle JP, Blackburn GL, *et al*. Eight-year weight losses with an intensive lifestyle intervention: the look AHEAD study. Obesity 2014;22(1):5-13.
8. Apovian CM, Aronne LJ, Bessesen DH, *et al*. Pharmacological management of obesity: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2015;100:342–362.
9. NIH conference. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. Ann Intern Med 1991;115(12):956–961.
10. Akkary E. Bariatric surgery evolution from the malabsorptive to the hormonal era. Obes Surg. 2012;22(5):827-31.
11. Knop FK, Taylor R. Mechanism of metabolic advantages after bariatric surgery. Diabetes Care 2013; 36(Supplement 2): S287-S291.
12. Gissey LC, Mariolo JRC, Mingrone G. How to Choose the Best Metabolic Procedure? Current Atherosclerosis Reports 2016; 18:43.
13. Angrisani L, Santonicola A, Iovino P, Formisano G, Buchwald H, Scopinaro. Bariatric Surgery Worldwide 2013. N.Obes Surg 2015;25(10):1822-32.
14. Silecchia G, Bacci V, Bacci S *et al*: Reoperation after laparoscopic adjustable gastric banding: analysis of a cohort of 500 patients with long-term follow-up. Surg Obes Relat Dis 2008;4(3):430–436
15. Schauer PR, Bhatt DL, Kirwan JP, *et al*. Bariatric surgery versus intensive medical therapy for diabetes – 3 year outcomes. N Engl J Med 2014;370:2002–2013.
16. Ikramuddin S, Korner J, Lee WJ, Connett JE, Inabnet WB, Billington CJ, *et al*. Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study randomized clinical trial. JAMA 2013;309:2240-9.
17. Kasama K, Mui W, Lee WJ, Lakdawala M, Naitoh T, Seki Y, Sasaki A, Wakabayashi G, Sasaki I, Kawamura I, Kow L, Frydenberg H, Chen A, Narwaria M, Chowbey P. IFSO-APC consensus statements 2011. Obes Surg. 2012;22(5):677-84.
18. O’Brien PE, Sawyer SM, Laurie C, Brown WA, Skinner S, Veit F, *et al*. Laparoscopic adjustable gastric banding in severely obese adolescents: A randomized trial. JAMA 2010;303:519-26.
19. Buchwald H, Estok R, Fahrbach K, *et al*. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 2009; 122:248–256.
20. Gumbs AA, Gagner M, Dakin G, *et al*. Sleeve gastrectomy for morbid obesity. Obes Surg 2007;17(7):962–969.
21. Himpens J, Dobbeleir J, Peeters G. Long-term results of laparoscopic sleeve gastrectomy for obesity. Ann Surg 2010; 252:319–324.
22. Scopinaro N, Gianetta E, Civalleri D, Bonalumi U, Bachi V. Biliopancreatic by-pass for obesity: II. Initial experience in man. British Journal of Surgery 1979;66(9):618–620.
23. Buchwald H, Oien DM. Metabolic/bariatric surgery Worldwide 2008. Obes Surg 2009; 19:1605–1611.
24. Sarwer B, Dilks RJ, Ritter S. Bariatric Surgery for Weight Loss. Encyclopedia of Body Image and Human Appearance. San Diego: Academic Press, 2012;1.
25. Gloy VL, Briel M, Bhatt DL, Kashyap SR, Schauer PR, Mingrone G, Bucher HC, Nordmann AJ. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ 2013;22:347.
26. Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Leccesi L, *et al*. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med 2012;366:1577-85.
27. Liang Z, Wu Q, Chen B, Yu P, Zhao H, Ouyang X. Effect of laparoscopic Roux-en-Y gastric bypass surgery on type 2 diabetes mellitus with hypertension: a randomized controlled trial. Diabetes Res Clin Pract. 2013;101(1):50-6.
28. Dixon JB, O’Brien PE, Playfair J, Chapman L, Schachter LM, Skinner S, *et al*. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. Obstet Gynecol Survey 2008;63:372-3.
29. Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, *et al*. Long-term mortality after gastric bypass surgery. N Engl J Med 2007;357:753-61.
30. Adams TD, Davidson LE, Litwin SE, Kolotkin RL, LaMonte MJ, Pendleton RC, *et al*. Health benefits of gastric bypass surgery after 6 years. JAMA 2012;308:1122-31.
31. Arterburn DE, Courcoulas AP. Bariatric surgery for obesity and metabolic conditions in adults. BMJ 2014 Aug 27;349:g396.
32. Buchwald H, Avidor Y, Braunwald E, *et al*. Bariatric surgery: a systematic review and meta-analysis. J Am Med Assoc 2004;292:1724–37.
33. Pournaras DJ, Aasheim ET, Søvik TT, *et al*. Effect of the definition of type II diabetes remission in the evaluation of bariatric surgery for metabolic disorders. Br J Surg 2012;99:100–103.
34. Ribaric G, Buchwald JN, McGlennon TW. Diabetes and weight in comparative studies of bariatric surgery vs conventional medical therapy: a systematic review and meta-analysis. Obes Surg. 2014;24:437-455.
35. Guo X, Liu X, Wang M, Wei F, Zhang Y, Zhang Y. The effects of bariatric procedures versus medical therapy for obese patients with type 2 diabetes: meta-analysis of randomized controlled trials. Biomed Res Int 2013;2013:410609.
36. Khanna V, Malin SK, Bena J, *et al*. Adults with long-duration type 2 diabetes have blunted glycemic and β-cell function improvements after bariatric surgery. Obesity 2015;23:523-526.
37. Schauer PR, Kashyap SR, Wolski K, *et al*. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med 2012;366:1567-1576.
38. Scopinaro N, Adami GF, Papadia FS, *et al*. The effects of biliopancreatic diversion on type 2 diabetes mellitus in patients with mild obesity (BMI 30-35 kg/m2) and simple overweight (BMI 25-30 kg/m2): a prospective controlled study. Obes Surg 2011; 21: 880-888.
39. Briatore L, Salani B, Andraghetti G, *et al*. Beta-cell function improvement after biliopancreatic diversion in subjects with type 2 diabetes and morbid obesity. Obesity 2010; 18: 932-936.
40. Scopinaro N, Adami GF, Papadia FS, *et al*. Effects of gastric bypass on type 2 diabetes in patients with BMI 30 to 35. Obes Surg 2014; 24: 1036-1043.
41. Hinojosa MW, Varela JE, Smith BR, Che F, Nguyen NT. Resolution of systemic hypertension after laparoscopic gastric bypass. J Gastrointest Surg 2009;13(4):793-7.
42. Sjostrom L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004;351:2683–93.
43. Dixon JB, O’Brien PE. Lipid profile in the severely obese: changes with weight loss after lap-band surgery. Obes Res 2002;10:903–10.
44. Dixon JB, Schachter LM, O'Brien PE, Jones K, Grima M, Lambert G, Brown W, Bailey M, Naughton MT. Surgical vs conventional therapy for weight loss treatment of obstructive sleep apnea: a randomized controlled trial. JAMA 2012;308(11):1142-9.
45. Mummadi RR, Kasturi KS, Chennareddygari S, Sood GK. Effect of bariatric surgery on non-alcoholic fatty liver disease: systematic review and meta-analysis. Clin Gastroenterol Hepatol 2008;6:1396–1402.
46. Karlsson J, Sjöström L, Sullivan M. Swedish obese subjects (SOS)—an intervention study of obesity. Two-year follow-up of health-related quality of life (HRQL) and eating behavior after gastric surgery for severe obesity. International Journal of Obesity 1998;22(2): 113–126.
47. Sjöström L, Gummesson A, Sjöström CD, *et al*. Swedish Obese Subjects Study. Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. Lancet Oncol 2009; 10(7): 653-62.
48. Sjostrom L, Narbro K, Sjostrom CD, *et al*. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med 2007;357:741–52.
49. Mingrone G, Greco AV, Giancaterini A, Scarfone A, Castagneto M, Pugeat M. Sex hormone-binding globulin levels and cardiovascular risk factors in morbidly obese subjects before and after weight reduction induced by diet or malabsorptive surgery. Atherosclerosis 2002;161(2):455-62.
50. Sugerman HJ, DeMaria EJ, Kellum JM, Sugerman EL, Meador JG, BSN, Wolfe LG. Effects of bariatric Surgery in Older Patients. Ann Surg. 2004; 240(2): 243–247.
51. Busetto L, Angrisani L, Basso N, *et al*. Safety and efficacy of laparoscopic adjustable gastric banding in the elderly. Obesity 2008;16:334–8.
52. Perry CD, Hutter MM, Smith DB, Newhouse JP, McNeil BJ. Survival and changes in comorbidities after bariatric surgery. Ann Surg 2008;247:21–7.
53. Fontaine KR, Barofsky I. Obesity and health related quality of life. Obes Rev 2001;2:173–82.
54. Miller ME, Kral J. Surgery for obesity in older women. Post reproductive health; Menopause International 2008; 14: 155–162.
55. Ochner CN, Teixeira J, Geary N, Asarian L. Greater Short-Term Weight Loss in Women 20-45 versus 55-65 Years of Age Following Bariatric Surgery. Obes Surg. 2013; 23(10): 1650–1654.
56. Belle SH, Berk PD, Chapman W, Christian N, Courcoulas AP, Dakin G, Flum DR, Horlick M, King WC, McCloskey C, Mitchell JE, Patterson E, Pender JR,Steffen K, Thirlby R,Wolfe B, Susan Yanovski S. Baseline characteristics of participants in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) study. Surg Obes Relat Dis. 2013; 9(6): 926–935.
57. Brethauer SA,Chand B, Schauer PR. Risks and benefits of bariatric surgery: Current evidence. CCJM 2006 Nov;73(11):993-1007.
58. Livingston EH. Procedure incidence and in-hospital complication rates of bariatric surgery in the United States. AmJ Surg 2004;188:105–10.
59. Cawley J, Meyerhoefer C. The medical care costs of obesity: an instrumental variables approach. J Health Econ. 2012;31(1):219-230.
60. McPherson K, Marsh T, Brown M. Foresight Tackling Obesities: Future Choices – Modelling Future Trends in Obesity and the Impact on Health. 2nd Edition.
61. The challenge of obesity in the WHO European region and the strategies for response. World Health Organization (Regional Office for Europe); Copenhagen: 2007.
62. Keating CL, Dixon JB, Moodie ML, *et al*. Cost-effectiveness of surgically induced weight loss for the management of type 2 diabetes: modelled lifetime analysis. Diabetes Care. 2009;32(4):567–574.
63. McEwen LN, Coelho RB, Baumann LM, Bilik D, Nota-Kirby B, Herman WH. The cost, quality of life impact, and cost-utility of bariatric surgery in a managed care population. Obes Surg. 2010;20(7):919–928.
64. Padwal R, Klarenbach S, Wiebe N, *et al*. Bariatric surgery: a systematic review of the clinical and economic evidence. J Gen Intern Med. 2011;26(10):1183–1194.
65. Hoerger TJ, Zhang P, Segel JE, Kahn HS, Barker LE, Couper S. Cost-effectiveness of bariatric surgery for severely obese adults with diabetes. Diabetes Care. 2010;33(9):1933–1939.
66. Neovius M, Narbro K, Keating C, *et al*. Health care use during 20 years following bariatric surgery. JAMA 2012;308(11):1132–1141.
67. SP, Padoin a V, Silva EN, *et al*. Economic benefits of bariatric surgery. Obes Surg. 2012;22(2):266–270.
68. Maciejewski ML, Livingston EH, Smith VA, Kahwati LC, Henderson WG, Arterburn DE. Health expenditures among high-risk patients after gastric bypass and matched controls. Arch Surg. 2012;147(7):633–640.
69. Weiner JP, Goodwin SM, Chang H-Y, *et al*. Impact of bariatric surgery on health care costs of obese persons: a 6-year follow-up of surgical and comparison cohorts using health plan data. JAMA Surg. 2013;148(6):555–562.
70. Tsesmeli N, Coumaros D. The future of bariatrics: endoscopy, endoluminal surgery, and natural orifice transluminal endoscopic surgery. Endoscopy 2010;42(2):155-62.