BENEFITS OF BARIATRIC SURGERY AND PERIOPERATIVE SURGICAL SAFETY

Ji Chung Tham,¹ *Carel W. le Roux^{2,3}

 General and Vascular Surgery Department, Musgrove Park Hospital, Taunton, UK
Diabetes Complications Research Centre, UCD Conway Institute, School of Medicine and Medical Science, University College Dublin, Dublin, Ireland
Gastrosurgical Laboratory, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
*Correspondence to carel.leroux@ucd.ie

Disclosure: The authors have declared no conflicts of interest. ORCHID number: 155215445 Received: 17.11.14 Accepted: 16.04.15 Citation: EMJ Diabet. 2015;3[1]:66-71.

ABSTRACT

Obesity is a worldwide problem with numerous associated health problems. The number of patients eligible for surgery outnumber surgical capacity and so patients need to be prioritised based on their obesity-related health burden and comorbidities. Weight loss as a result of bariatric surgery is significant and maintained in the long term. In addition to weight loss, patient health improves in terms of metabolic, macrovascular, and microvascular disease. As a result, quality of life is better, along with psychosocial wellbeing. Bariatric surgery is associated with a relatively low number of complications and appears to result in a reduction in mortality risk due to the resolution of comorbidities. Hence, surgery can now be routinely considered as an adjunct to medical therapy in the management of obesity.

Keywords: Bariatric, long-term, safety, metabolic.

INTRODUCTION

Obesity is a pandemic¹ with several treatment from education. strategies ranging health promotion, medical therapy, and surgery attempting to control the problem. The projected healthcare burden to many healthcare services may be unsustainable in terms of both cost and morbidity.^{2,3} Hence, strategies that provide more sustainable and reproducible results, such as intensive medical therapy and surgery, are becoming the interventions of choice.

Bariatric surgery encompasses a group of surgical procedures, which include the adjustable gastric band (AGB), vertical sleeve gastrectomy (VSG), Roux-en-Y gastric bypass (RYGB), and biliopancreatic diversion (± duodenal switch) (BPD); all of which are aimed at improving patient health. AGB and RYGB were the most common bariatric operations conducted internationally, but the popularity of VSG has dramatically increased during the last 4 years. Currently, bariatric surgery is only offered to patients with a body mass

index (BMI) >40 kg/m² or to those with a BMI >35 kg/m² with obesity-related comorbidities.⁴ BMI has its limitations and does not reflect the true composition of fat versus lean tissue. Anthropometric measurement using dual-energy X-ray absorptiometry or magnetic resonance imaging is a better measure of body composition but the actual metabolic or health risk of obesity is not portrayed by its results. The Edmonton Obesity Staging System and the King's Obesity Staging Score classify obesity based on comorbidities to predict risk of mortality independent of weight.5,6 These systems are ideal as they prioritise patients for treatment in terms of severity of health burden and may also identify individuals who will benefit more from interventions. It is essential to ensure that treatments offered to individuals produce not only the desired outcomes but are also safe in the long term. This review attempts to highlight the effectiveness, perioperative, and long-term safety of bariatric surgery based on current evidence.

Effectiveness of Bariatric Surgery -Weight Change

Initial studies raised issues of weight regain after surgery.7-9 These results fuelled the idea that surgery is a 'temporary fix' to the obesity problem. Surgery results in physiological changes to the body¹⁰ that lead to sustained weight loss, albeit with an initial small regain in weight.¹¹ Data from the Swedish Obese Subjects (SOS) study, which includes >4,000 patients and 20 years of followup, show that weight loss is maintained in most patients after bariatric surgery, with greatest effect after RYGB compared with gastric banding and vertical banded gastroplasty.¹¹ The effect of weight loss resulted in profound improvements in physiology, psychosocial function, and guality of life (QoL). When patients were divided using growth mixture models, distinct, differing patterns of weight loss could be detected; each showed different weight loss and weight regain trajectories, suggesting the presence of preoperative characteristics that can predict final outcome.¹² These factors could possibly be reversible or treated, and hence should be identified prior to surgery.

Effectiveness of Bariatric Surgery - Metabolic

Immediately after VSG and RYGB, improvement in insulin resistance (IR) and an exaggerated postprandial insulin response occur; outcomes that are not present immediately after AGB.^{13,14} Improvement in diabetes control is sustained for up to 3 years, as shown by randomised controlled trials, and appears to be superior to lifestyle and medical therapy, with 44% of patients achieving a glycated haemoglobin of <6.0% (42 mmol/mol) without the need for medication, which satisfies the definition of the American Diabetes Association for remission of Type 2 diabetes mellitus (T2D).¹⁵ Additionally, the SOS study showed that glycaemic control in those with T2D pre-surgery remains adequate at 20 years postoperatively, with post-bariatric patients having lower baseline levels of insulin and/or lower blood glucose levels. Despite these improvements, many may relapse into mild or controlled T2D in the long term.¹⁶ The SOS trial also demonstrates improvements in glycaemic control in AGB patients, although to a lesser extent. Very significant improvements in glucose homeostasis are seen after BPD in patients followed for 10 years.¹⁷ Significantly, in conjunction with medical therapy, bariatric surgery provides better glycaemic control than medical therapy

alone or than surgery alone.¹⁸ Therefore, for the long-term treatment of diabetes, bariatric surgery in combination with best medical therapy should be considered as a viable and probably superior option to either intervention on its own.

Effectiveness of Bariatric Surgery – End-Organ Macrovascular Damage

Diabetes, as part of the metabolic syndrome and obesity, results in end-organ damage such as atherosclerosis, myocardial infarction, and stroke. Hence, it is unsurprising that the risk of cardiovascular (CV) events decreases over time as metabolic control of diabetes improves. RYGB as an adjunct to intensive medical therapy results in improvements in glycaemic control, high-density lipoprotein cholesterol levels, triglyceride levels, blood pressure, and requiring fewer medications to achieve optimal metabolic control.¹⁵ However, the underlying mechanism is unclear and it is debated whether results are solely due to weight loss.

Surprisingly, intensive lifestyle interventions have similar outcomes in terms of CV events compared with usual care in patients with a mean BMI of 36.0 kg/m² and T2D, despite weight loss of 6.0% in the intensive arm versus 3.5% in controls at 10 years.¹⁹ Therefore, modest weight loss through diet and exercise on its own does not contribute to significant CV benefit. Treatment of patients with high baseline insulin levels and not high BMI was significantly correlated to reduction in risk of CV events after bariatric surgery.¹¹ Therefore, bariatric surgery can be offered to patients with significant IR or diabetes to reduce future morbidity or mortality, although heavier patients with no IR may not benefit as much.

Effectiveness of Bariatric Surgery – End-Organ Microvascular Damage

End-organ microvascular damage such as retinopathy, neuropathy, and nephropathy can occur with diabetes. Improved glycaemic and metabolic control may halt progression.²⁰⁻²² Various methods of assessing renal function include measuring creatinine to estimate glomerular filtration rate (eGFR), while assessment of renal damage relies on the degree of elevation of urinary albuminto-creatinine ratio (ACR). The use of eGFR as a measure of improvement in renal function is not ideal in bariatric surgery because of the loss in lean muscle mass and the subsequent reduction in creatinine.²³

laconelli et al.¹⁷ observed that 10 years after BPD, patients recovered from microalbuminuria and had preserved renal function compared with a control group treated with best medical care who had progressive kidney damage and deteriorating renal function. These results suggest that bariatric surgery may potentially reverse glomerular damage, and this can be seen after RYGB, with mean urinary ACR improving from 7.6 to 2.2 mg/mmol.²⁴ In a similar context, diabetic retinopathy results in ophthalmological microaneurysms, cottonwool spots, flame haemorrhages, pathological angiogenesis, and blindness. Mean retinopathy scores may improve after bariatric surgery, although at a slower rate than urinary ACR, suggesting that longer follow-up is needed to see these changes.²⁴⁻²⁶ Using nerve conduction studies, the same group also showed that neither deterioration nor improvement can be detected at 1 year after RYGB.²⁶

Effectiveness of Bariatric Surgery – Psychosocial and QoL

Improvements in weight may lead to the assumption that physical activity will increase. One of the Longitudinal Assessment of Bariatric Surgery (LABS) reports noted that although physical activity of postoperative patients did increase on average, a significant number of patients (up to 29%) were less active when compared with their preoperative state.²⁷ King et al.²⁷ proposed that the likely explanation may be secondary to ongoing pain from osteoarthritis or that patients still have their physical activities limited by asthma, and these problems may not have been altered in their progressive nature. An alternative hypothesis is that with the weight loss after bariatric surgery the motivation for these patients to be physically active to control their weight has diminished.

One would also expect that the mental wellbeing of patients recovers as their health improves after bariatric surgery. Observations from the LABS study, using the Beck depression inventory, showed that the risk of a major adverse event (AE) such as clinical depression within 30 days of surgery was increased, but the overall number of patients with depression significantly improved at 1 year. However, after the peak improvement was reached at 1 year, a small but significant deterioration occurred from Year 1 to 3.²⁸ Moreover, a large study of 19,577 patients with 7 years follow-up showed that although post-RYGB patients had an overall significant reduction in mortality, rate of death due to suicide was 1.58-times greater.²⁹ Alcohol use disorder (AUD) also increased 2 years after RYGB but not AGB.³⁰ The underlying reason is unclear but may lie in the changes in alcohol absorption and reward centres in the brain that occur in RYGB patients but not in AGB patients. King et al.³⁰ also found that the risk of postoperative AUD was associated with male sex, younger age, regular substance abuse prior to surgery, and lower interpersonal support. Further studies are necessary to understand the underlying mechanism in order to treat the problem.

In terms of QoL, Schauer et al.¹⁸ found that RYGB and VSG patients had better physical function, higher energy levels, and perception of better general health at 3 years after surgery compared with patients on medical therapy. The assessment of QoL was based on the RAND 36-item health survey, which is a modification of the short form (SF)-36 survey. In intensive medical therapy patients, no significant improvements in QoL were found, while 5 of 8 mental and physical domains in RYGB patients and 2 of 8 domains in VSG patients showed significant improvements.¹⁸ It is likely that improvements in the CV function of the postbariatric surgery patient explains better physical function and energy levels, as patients are able to perform more physical activities²⁷ and feel less tired. Improvements in health from chronic diseases and the reduction in medication use may allow patients to no longer feel 'tied down' by their conditions and thus create the perception of better health.

Effectiveness of Bariatric Surgery and its Failure

In the event that the surgical procedure fails to produce its effect or produces unwanted effects, reversal or revision surgery can be performed. The rate of revision for AGB appears to evolve with the learning curve, with O'Brien et al.³¹ showing its rate dropping from 40% within 10 years to 6.4% thereafter. Usual causes for revision include complications such as erosion, proximal dilatation, and band problems.³¹ VSG cannot be reversed but can be revised and it occurs at a rate of 8.2-9.4% in short-term follow-up.^{32,33} The reasons for revision include reflux, dysphagia, and/or poor weight outcome.^{32,33} For RYGB, revision surgery is complex and difficult with high complication rates,³⁴ but the revision rates are low at 0-1.6%.^{32,35} The most common reason for revision is severe hypoglycaemia.³⁵

Complication	Roux-en-Y gastric bypass, %	Vertical sleeve gastrectomy, %	Adjustable gastric banding, %
Anastomotic leak	0.19-0.7838-41	0-0.7440,41	-
Intestinal obstruction	0.35-0.95 ³⁸⁻⁴¹	0-0.1240,41	-
Stricture/stenosis	0.15-1.4238,40	0.4240	0.13 ⁴⁰
Haemorrhage	1.11-3.4238-41	0.59-0.6440,41	0.05-0.1340,41
Deep vein thrombosis and/or pulmonary embolism	0.05-0.9437-41	0.32-0.9440,41	0.07-0.3037,40,41
Pneumonia	0.13-0.2338, 40	0.11 ⁴⁰	0.0240
Reoperations	1.30-5.0237-41	0.59-2.9740,41	0.63-0.9237,40,41
Total complications	2.8-10.337-41	5.61-5.90 ^{40,41}	1.00-2.3037,40,41

For BPD, reversal usually occurs after a trial of revision surgery and is between 2-7%. $^{\rm 36}$

PERIOPERATIVE AND LONG-TERM MORBIDITY AND MORTALITY OF BARIATRIC SURGERY

Perioperative and 30-Day Morbidity and Mortality

In the perioperative setting, numerous studies have shown that bariatric surgery is associated with a relatively low risk of complications compared with other surgical interventions of similar complexity.^{18,37} According to Flum et al.,³⁷ 30-day mortality from AGB is close to 0% and mortality from RYGB close to 0.2%. The overall 30-day complication rate is 1% for AGB and 4.8% for RYGB, with a reoperation rate within 30 days for AGB of 0.8% and 3.2% for RYGB.³⁷ In a broader aspect, the 30-day mortality rate of RYGB in two large European studies ranges from 0.04-0.1%, 38, 39 while large North American studies range from 0.14-0.2%.^{12,37,40,41} From these North American studies, 30-day mortality from AGB ranges from 0-0.11%, while that of VSG ranges from 0-0.05%.^{37,40,41} The SOS study had an overall 90-day mortality rate of 0.25%⁹ and from a recent meta-analysis the 30-day mortality was 0.08%.42

Thirty-day complications for RYGB range from 2.8-10.3%.³⁷⁻⁴¹ An anastomotic leak is the most feared complication as it results in grave morbidity and requires reoperation. Anastomotic leak rate ranges from 0.19–0.78% with most requiring reoperation.³⁸⁻⁴¹ See Table 1 for a list of complications of RYGB, VSG, and AGB. Serious complications are ones that usually require reoperation and seem to be highest with RYGB followed by VSG, then AGB. Even though it has been noted that outcomes and complications of VSG usually lie between RYGB and AGB, patients receiving VSG had the highest rate of deep vein thrombosis and/or pulmonary embolism. The underlying reason is yet to be elucidated.

At 1-year follow-up, the complication rate for RYGB is 30%, with 10% directly related to surgery (strictures, bleeding, and obstruction), but without significant differences compared with AEs in medical therapy patients.¹⁵ At 3-year follow-up, 0.1-0.9% of RYGB patients require subsequent bariatric surgery procedures for late complications compared with 13.8-21.9% in AGB patients in the LABS study.¹² In a 5-year follow-up study, the late complication rate for RYGB was 16.1%.43 In longterm follow-up of up to 16 years, the risk of mortality is lower in the post-bariatric surgery patient compared with patients that did not have surgery, despite the risk of surgical complications,⁹ suggesting that, overall, bariatric surgery improves survival. In the SOS study, of which the follow-up data for each patient was for \geq 10 years, 31% of AGB and 17% of RYGB patients required reoperations or conversions to a different bariatric procedure.44 Currently, there are no high-quality cohort followup data for reoperations or conversions for VSG.

Apart from BPD, none of the procedures discussed cause clinically significant macronutrient malabsorption, but in VSG and RYGB micronutrient deficiencies do occur as a result of altered anatomy and physiology. Common deficiencies that occur include iron and vitamins A, B, D, and E.⁴⁵ At 1 year, VSG patients are more iron-deficient compared with RYGB patients (30% versus 20%, respectively). However, RYGB patients are more

deficient in vitamins A (23%), B12 (17%), and D (83%) compared with VSG patients (20%, 7%, and 70%, respectively).⁴⁵ Interestingly, vitamin D deficiency is prevalent preoperatively; whilst RYGB results in no vitamin D improvement, VSG results in almost 50% fewer patients with deficiency at 1 year.⁴⁶ In BPD, significant malabsorption does occur and requires revision and/or reversal in 3-18.5%.³⁶ Common nutrients that are deficient include vitamin A, calcium, and iron.⁴⁷ One needs to bear in mind that all BPD patients receive nutritional supplements and an altered diet postoperatively; therefore, exact quantification of nutrient deficiency is difficult. Hence, it is vital to closely monitor nutrient status in all post-bariatric surgery patients.

Postprandial hypoglycaemia may occur 90–120 mins postprandially after VSG and RYGB but should be distinguished from the dumping syndrome, which is a condition characterised by a constellation of symptoms due to autonomic hyperstimulation that usually occur within minutes of consuming high-glycaemic-index foods. The Bariatric Outcomes Longitudinal Database (BOLD) study⁴⁸ showed that only 0.1% of patients have incidences of selfreported hypoglycaemia. However, not all patients with low serum glucose present with symptoms.⁴⁹ Management of postprandial hypoglycaemia includes simple dietary adjustments: frequent but small and low-glycaemic-index carbohydrate meals, or pharmacological management with medication that reduces carbohydrate absorption, inhibits insulin release, or inhibits gastrointestinal hormones.⁵⁰ Surgical management should be a last resort, as revision or reversal surgery carries a very high risk of complications.³⁴ No high-level evidence has shown that symptomatic patients require revision surgery. The presentation of dumping syndrome is regularly seen in follow-up clinics but occurs fairly rarely (0.2%).⁵¹

CONCLUSION

Long-term data for bariatric surgery indicate that it is a useful adjunct to medical and lifestyle management of morbidly obese patients with complications due to obesity. Care must be taken to select appropriate candidates and then to support them in the long term. The effectiveness of bariatric surgery in the management of morbid obesity is further supported by good long-term safety profiles. Surgery should now be routinely considered in combination with medical therapy to help patients who suffer the consequences of obesity.

REFERENCES

1. World Health Organization. Obesity and overweight. Fact sheet No. 311. Updated January 2015. Available at: http://www. who.int/mediacentre/factsheets/fs311/ en/. Last Accessed: 1 October 2014.

2. Butland B et al. Tackling Obesities: future choices - project report (2nd edition). UK Government's Foresight Programme, Government Office for Science. 2007.

3. OECD. Health at a Glance: Europe 2010. OECD Publishing. 2010.

4. McEwen J et al. Obesity: Guidance on the prevention of overweight and obesity in adults and children. NICE clinical guideline 43. 2006. Available at: http://www.nice.org.uk/guidance/cg43/ resources/guidance-obesity-pdf. Last accessed: 6 August 2015.

5. Padwal RS et al. Using the Edmonton obesity staging system to predict mortality in a population-representative cohort of people with overweight and obesity. CMAJ. 2011;183(14):E1059-66.

6. Aasheim ET et al. Assessment of obesity beyond body mass index to determine benefit of treatment. Clin Obes. 2011;1(2-3):77-84.

7. Suter M et al. European experience with laparoscopic Roux-en-Y gastric bypass in 466 obese patients. Br J Surg. 2006;93(6):726-32.

8. Ballesta-López C et al. Learning curve for laparoscopic Roux-en-Y gastric bypass with totally hand-sewn anastomosis: analysis of first 600 consecutive patients. Surg Endosc. 2005;19(4):519-24.

9. Sjöström L et al; Swedish Obese Subjects Study. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007;357(8): 741-52.

10. Tham JC et al. The role of bariatric surgery in the treatment of diabetes. Ther Adv Chronic Dis. 2014;5(3):149-57.

11. Sjöström L et al. Bariatric surgery and long-term cardiovascular events. JAMA. 2012;307(1):56-65.

12. Courcoulas AP et al; Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. JAMA. 2013;310(22):2416-25.

13. le Roux CW et al. Gut hormone profiles

following bariatric surgery favor an anorectic state, facilitate weight loss, and improve metabolic parameters. Ann Surg. 2006;243(1):108-14.

14. Papamargaritis D et al. Changes in gut hormone profile and glucose homeostasis after laparoscopic sleeve gastrectomy. Surg Obes Relat Dis. 2013;9(2):192-201.

15. Ikramuddin S 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(21):2240-9.

16. Sjöström 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(3):219-34.

17. laconelli A et al. Effects of biliopancreatic diversion on diabetic complications: a 10-year follow-up. Diabetes Care. 2011;34(3):561-7.

18. Schauer PR et al. Bariatric surgery versus intensive medical therapy for diabetes--3-year outcomes. N Engl J Med. 2014;370(21):2002-13.

19. Wing RR et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med. 2013;369(2): 145-54.

20. Gaede P et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med. 2003;348(5):383-93.

21. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet. 1998;352(9131):854-65.

22. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352(9131):837-53.

23. Lieske JC et al. Gastric bypass surgery and measured and estimated GFR in women. Am J Kidney Dis. 2014;64(4): 663-5.

24. Miras AD et al. Bariatric surgery does not exacerbate and may be beneficial for the microvascular complications of type 2 diabetes. Diabetes Care. 2012;35(12):e81.

25. Klein R et al. An alternative method of grading diabetic retinopathy. Ophthalmology. 1986;93(9):1183-7.

26. Miras AD et al. Type 2 diabetes mellitus and microvascular complications 1 year after Roux-en-Y gastric bypass: a case-control study. Diabetologia. 2015;58(7):1443-7.

27. King WC et al. Pre- to postoperative changes in physical activity: report from the longitudinal assessment of bariatric surgery-2 (LABS-2). Surg Obes Relat Dis. 2012;8(5):522-32.

28. Mitchell JE et al. Course of depressive symptoms and treatment in the longitudinal assessment of bariatric surgery (LABS-2) study. Obesity (Silver Spring). 2014;22(8):1799-806.

29. Adams TD et al. Long-term mortality after gastric bypass surgery. N Engl J Med. 2007;357(8):753-61.

30. King WC et al. Prevalence of alcohol

use disorders before and after bariatric surgery. JAMA. 2012;307(23):2516-25.

31. O'Brien PE et al. Long-term outcomes after bariatric surgery: fifteen-year followup of adjustable gastric banding and a systematic review of the bariatric surgical literature. Ann Surg. 2013;257(1):87-94.

32. Dogan K et al. Effectiveness and Safety of Sleeve Gastrectomy, Gastric Bypass, and Adjustable Gastric Banding in Morbidly Obese Patients: a Multicenter, Retrospective, Matched Cohort Study. Obes Surg. 2015;25(7):1110-8.

33. van Rutte PW et al. Outcome of sleeve gastrectomy as a primary bariatric procedure. Br J Surg. 2014;101(6):661-8.

34. Vilallonga R et al. Laparoscopic reversal of Roux-en-Y gastric bypass into normal anatomy with or without sleeve gastrectomy. Surg Endosc. 2013;27(12):4640-8.

35. Himpens J et al. Long-term results of laparoscopic Roux-en-Y Gastric bypass: evaluation after 9 years. Obes Surg. 2012;22(10):1586-93.

36. Topart PA, Becouarn G. Revision and reversal after biliopancreatic diversion for excessive side effects or ineffective weight loss: a review of the current literature on indications and procedures. Surg Obes Relat Dis. 2015;11(4):965-72.

37. Flum DR et al. Perioperative safety in the longitudinal assessment of bariatric surgery. N Engl J Med. 2009;361(5): 445-54.

38. Dillemans B et al. Standardization of the fully stapled laparoscopic Roux-en-Y gastric bypass for obesity reduces early immediate postoperative morbidity and mortality: a single center study on 2606 patients. Obes Surg. 2009;19(10):1355-64.

39. Jacobsen HJ et al. High-volume bariatric surgery in a single center: safety, quality, cost-efficacy and teaching aspects in 2,000 consecutive cases. Obes Surg. 2012;22(1):158-66.

40. Hutter MM et al. First report from the American College of Surgeons Bariatric Surgery Center Network: laparoscopic sleeve gastrectomy has morbidity and effectiveness positioned between the band and the bypass. Ann Surg. 2011;254(3):410-20; discussion 420-2.

41. Birkmeyer NJ et al. Hospital complication rates with bariatric surgery in Michigan. JAMA. 2010;304(4):435-42.

42. Chang SH et al. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003-2012. JAMA Surg. 2014;149(3): 275-87.

43. Schauer PR et al. Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. Ann Surg. 2003;238(4):467-84; discussion 84-5.

44. Sjöström L et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(26):2683-93.

45. Coupaye M et al. Comparison of nutritional status during the first year after sleeve gastrectomy and Roux-en-Y gastric bypass. Obes Surg. 2014;24(2):276-83.

46. Vix M et al. Impact of Roux-en-Y gastric bypass versus sleeve gastrectomy on vitamin D metabolism: short-term results from a prospective randomized clinical trial. Surg Endosc. 2014;28(3): 821-6.

47. Marceau P et al. Long-Term Metabolic Outcomes 5 to 20 Years After Biliopancreatic Diversion. Obes Surg. 2015;25(9):1584-93.

48. Sarwar H et al. Hypoglycemia after Roux-en-Y gastric bypass: the BOLD experience. Obes Surg. 2014;24(7):1120-4.

49. Laurenius A et al. More symptoms but similar blood glucose curve after oral carbohydrate provocation in patients with a history of hypoglycemia-like symptoms compared to asymptomatic patients after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2014;10(6):1047-54.

50. Foster-Schubert KE. Hypoglycemia complicating bariatric surgery: incidence and mechanisms. Curr Opin Endocrinol Diabetes Obes. 2011;18(2):129-33.

51. Marsk R et al. Nationwide cohort study of post-gastric bypass hypoglycaemia including 5,040 patients undergoing surgery for obesity in 1986-2006 in Sweden. Diabetologia. 2010;53(11): 2307-11.