Acta Diabetol (2013) 50:475–478
DOI 10.1007/s00592-013-0453-2

REVIEW ARTICLE

# Preoperatively determinable factors predictive of diabetes mellitus remission following Roux-en-Y gastric bypass: a review of the literature

**ST Adams · M. Salhab · ZI Hussain · GV Miller · SH Leveson**

Received: 23 July 2012 / Accepted: 11 January 2013 / Published online: 7 March 2013


**Abstract** It is well established that weight loss in general and bariatric surgery in particular can improve glycaemic control in diabetics. Current NICE guidelines recommend that those patients with type 2 diabetes mellitus and a BMI of 35 kg/m$^2$ or more should be considered for bariatric surgery in order to optimise their glycaemic control and minimise their risk of long-term complications. The commonest bariatric procedure in the UK is the Roux-en-Y gastric bypass that has been shown to result in long-standing type 2 diabetes resolution in 83 % of patients. Since such surgery carries a small but significant risk of mortality, as well as posing considerable lifestyle implications for the patient, numerous studies have been performed with a view to identifying which patients and which procedures are most likely to result in these desired benefits. This paper summarises the existing literature on this topic.

**Keywords** Obesity · Diabetes · Bypass

## Introduction

One of the main benefits of bariatric surgery is that it has been shown to reduce the severity of type 2 diabetes mellitus (DM), in some cases inducing remission lasting several years [1–3]. Indeed, the non-medical media has often touted bariatric surgery as a "cure" for diabetes although specialist medical opinion has tended to shy away from using this term [4]. The mechanisms by which such procedures result in prolonged improvement in glycaemic control have been the subject of a great deal of study with weight loss, reduced oral intake, altered hormonal secretion and changes to the gastrointestinal tract microflora all having been proposed as playing a part in this phenomenon [5–11]. Given the serious nature of the complications of DM on the cardiovascular and renal systems, the level of interest in the effects of bariatric surgery on such pathologies is perhaps unsurprising [3, 12–15].

A consensus statement released in 2009 by a panel of expert endocrinologists defined remission of type 1 and type 2 DM as glycaemia below the diabetic range in the absence of pharmacological or surgical therapy [4]. Partial remission was defined as sub-diabetic hyperglycaemia (HbA1c <6.5 %, fasting glucose 5.6–6.9 mmol/l (or ≥99 and ≤126 mg/dl)) of at least 1 year's duration, and complete remission was defined as a full return to normal measures of glucose metabolism (normal HbA1c, fasting glucose <5.6 mmol/l) for the same duration [4]. Prolonged remission was considered to be complete remission lasting 5 or more years [4].

## Bariatric surgery in diabetics

Presently, 366 million people worldwide are thought to be affected by DM [16]. A large proportion of these people are also obese and therefore eligible for potential remission inducing bariatric surgery. A meta-analysis by Buchwald et al. [1] looking at bariatric surgery as a whole showed complete remission of type 2 DM at 2-year follow-up in 78.1 % of patients and improvement in a further 8.5 %

Communicated by Antonio Secchi.

S. Adams (✉) · M. Salhab · Z. Hussain · G. Miller · S. Leveson
Department of General Surgery, York Hospital, Wigginton Road, York YO318HE, UK
e-mail: rpbgt@hotmail.com

with excess bodyweight loss (eBWL) and DM remission rates being greatest in the duodenal switch patients, then in the Roux-en-Y gastric bypass (RYGBP) patients and worst in those undergoing gastric banding. Similar results were reported in a systematic review by Meijer et al. [3] which showed DM remission in 83 % of RYGBP patients and 62 % of gastric band patients at 2–14-year follow-up. Although most of the literature on this topic has focused on results over the first few postoperative years, those few studies with longer follow-up periods have shown that the phenomenon of DM remission persists—for example, Pories et al. [17] reported a case series in which 82.9 % of previously diabetic patients who had undergone RYGBP had normal glucose homoeostasis parameters at 10–14 years [2, 17–18]. It should be noted, however, that all of these papers refer to the data either published or collected prior to the publication of the revised criteria for DM remission described above. The reason why this may be significant is that Pournaras et al. [19] presented data in 2011 in which patients showed only a 34 % complete DM remission rate at 1 year according to the new criteria (41 % for RYGBP, 26 % for sleeve gastrectomy and 7 % for gastric banding) suggesting that a revision of the expectations post-bariatric surgery may be necessary for patients and clinicians alike.

Given the impressive results in the obese population with DM, it is perhaps unsurprising that recently attention has been paid to determining whether or not other groups of diabetics would experience similar benefits. To date, the only study to investigate the effects of RYGBP on obese patients with type 1 DM reported that 4 of the 5 patients with the condition (out of 2,170 in the series) experienced a reduction in insulin requirements at 3–76 months follow-up (mean 29 months) [20]. Their mean eBWL was 58.9 % (range 47.1–82 %) [20]. Clearly, however, the numbers involved in this study make it difficult to draw any firm conclusions. In stark contrast, however, there is increasing evidence to suggest that patients with type 2 DM with body mass indexes (BMIs) below the current cut-off point for bariatric surgery as defined by NICE guidelines may benefit more than initially thought [21, 22]. A review of the literature published by Reis et al. [23] found that improvements in glycaemic control in the BMI <35 group were seen with a range of different bariatric techniques.

## Predictors of remission

### Short term

In comparison with studies looking primarily at eBWL, there is a relative paucity of studies attempting to identify predictive factors for the remission of DM. The best attempt to establish a predictive model for this issue was published by Hayes et al. in 2011 [24]. Hayes et al. [24] used 13 preoperative parameters and a variety of statistical and data mining techniques to create 6 different mathematical models [24]. These models were able to correctly identify which patients would experience remission of their DM at 12 months follow-up in 82.7–87.4 % of cases. The most accurate model was a decision tree based on DM status (unrecognised, diet controlled, tablet controlled or insulin controlled), fasting glucose levels, HbA1c, and whether or not the patient had concomitant hypertension [24]. The two strongest predictors of DM resolution were low HbA1c and no requirement for insulin therapy which were used in all 6 of the models and were the only factors used for 3 of them [24]. These two factors alone successfully predicted DM remission in 86.6 % of cases in 2 of these 3 models [24]. Interestingly, Hayes et al. [24] also found that a lower preoperative BMI was a negative predictor of DM resolution which clearly could have important implications for clinicians with regard to patient selection and the indications for surgery.

Another study addressing the issue of prediction of DM remission would be Hamza et al. [25] who reported that the percentage of postoperative eBWL was the only predictor of DM remission influenced by the choice of procedure and that the only other independent predictor was younger age. The finding that greater eBWL results in improved DM remission rates echoes that of a previous study by Kadera et al. [26] although clearly this finding is of little relevance to those seeking to predict DM remission in preoperative patients. Similar findings regarding patient age were presented by Lee et al. [27] who proposed that not only did younger age confer an increased chance of DM remission but also that having a shorter duration of DM was an independent predictor. This finding too has been supported in subsequent studies [26, 28].

Other factors which have been found to be significantly associated with the chances of DM remission following RYGBP include the nature and level of preoperative DM control. Several studies, including Maciejewski et al. [29], have reported that those RYGBP patients most likely to have discontinued their DM medication at 1 year postoperatively were those who were treated preoperatively with oral hypoglycaemic agents alone, followed by those on insulin alone and lastly those on both forms of treatment [30]. Kadera et al. [26] went one step further and suggested that not only did insulin requirement *per se* significantly influence the chances of remission versus mere improvement of DM control but also that insulin dose significantly differed between the 2 groups. It is perhaps noteworthy that although all 6 of the models proposed by Hayes et al. [24] used preoperative HbA1c in their analyses, other studies have found no significant association between this factor and DM remission [26]. Similarly, whilst Hall et al. [28]

reported a significant difference in remission rates between those with a preoperative HbA1c >10 % compared to those for whom it was between 6.5 and 7.9 %, the lowest rate of DM remission was seen in those patients whose levels fell between these two groups. It has been proposed that a more predictive accurate measurement would be the homeostatic model of assessment estimated glucose disposition index (HOMA-DI), which is the product of insulin sensitivity and beta-cell sensitivity; however, presently, this measurement is not in common use, and there is little evidence in the literature to support this suggestion [31, 32].

Long term

As discussed in the opening paragraph, the term "remission of diabetes" is preferred to the use of the word "cure" as it implies the potential for the re-emergence of abnormal glucose homoeostasis in the future. To date, there exist only a handful of papers looking at predictive factors for the long-term durability of DM remission. Chikunguwo et al. [33] investigated 157 patients whose type 2 DM had gone into remission at 1-year post-RYGBP and found that prolonged remission existed in 57 % of them. Echoing the conclusions of studies looking at short-term remission, they found that durable remission was most likely in those patients whose DM was initially controlled by diet alone, followed by those on oral hypoglycaemic agents alone and finally by those requiring insulin [33]. Prolonged DM remission was also significantly more likely in men than in women [33]. Low eBWL, weight regain and older age were weak predictors of remission [33]. In a similar but smaller study using a shorter follow-up period, DiGiorgi et al. [34] found comparable results to Chikunguwo et al. [33] in terms of reduced durability of remission in those patients who experienced less postoperative eBWL or weight regain (Table 1).

One potential confounding factor common to each of the above studies is that it is assumed that the patients in the study populations had type 2 DM rather than latent autoimmune diabetes of the adult (LADA) [35]. LADA is a form of type 1 DM in which there is gradual autoimmune destruction of the pancreatic beta-cells over a period of up to 12 years rather than the peripheral insulin resistance characteristic of type 2 DM [35, 36]. Because of the slow progression of the disease, many patients are erroneously diagnosed with type 2 DM, whereas in actuality in 10 % of the phenotypically type 2 DM, population over age the age of 35 and 25 % of those below it LADA is the true diagnosis [35, 36].

**Table 1** Showing preoperative predictors of DM remission following RYGBP in the short and long terms

| | Positively associated with DM remission | Negatively associated with DM remission |
|---|---|---|
| Short term | Mode of DM control (diet > tablet > insulin (low dose > high dose)) | Lower preoperative BMI |
| | Good glycaemic control (fasting glucose/HbA1c) | Concomitant hypertension |
| | Younger age at surgery | |
| | Shorter duration since onset of DM | |
| Long term | Mode of DM control (diet > tablet > insulin) | |
| | Gender (male > female) | |

## Summary

Whilst it seems to be universally accepted that all forms of surgical and non-surgical BWL improve type 2 DM, albeit to varying degrees, the exact mechanisms by which they do this remain a source of controversy. There is strong evidence to support the idea that the less severe and short-lived a patient's DM is then the greater their chances of achieving a sustained, complete remission following surgery. Whether or not there are any other predictive factors that could be used to identify those individuals most likely to benefit from surgically induced BWL is presently unknown.

## References

1. Buchwald H, Estok R, Fahrbach K et al (2009) Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 122(248–256):e245
2. Fobi MA (2010) P-119 Is the effect of gastric bypass on type 2 diabetes permanent? 27th Annual Meeting of the ASMBS, Las Vegas, Nevada, US, p s67
3. Meijer RI, van Wagensveld BA, Siegert CE, Eringa EC, Serne EH, Smulders YM (2011) Bariatric surgery as a novel treatment for type 2 diabetes mellitus: a systematic review. Arch Surg 146:744–750
4. Buse JB, Caprio S, Cefalu WT et al (2009) How do we define cure of diabetes? Diabetes Care 32:2133–2135
5. Burcelin R, Serino M, Chabo C, Blasco-Baque V, Amar J (2011) Gut microbiota and diabetes: from pathogenesis to therapeutic perspective. Acta Diabetol 48:257–273
6. Amar J, Serino M, Lange C et al (2011) Involvement of tissue bacteria in the onset of diabetes in humans: evidence for a concept. Diabetologia 54:3055–3061
7. Ishida RK, Faintuch J, Paula AM et al (2007) Microbial flora of the stomach after gastric bypass for morbid obesity. Obes Surg 17:752–758
8. Dixon JB, le Roux CW, Rubino F, Zimmet P (2012) Bariatric surgery for type 2 diabetes. Lancet 379:2300–2311
9. Pournaras DJ, Osborne A, Hawkins SC et al (2010) Remission of type 2 diabetes after gastric bypass and banding: mechanisms and 2 year outcomes. Ann Surg 252:966–971
10. Thaler JP, Cummings DE (2009) Minireview: hormonal and metabolic mechanisms of diabetes remission after gastrointestinal surgery. Endocrinology 150:2518–2525

11. Vetter ML, Ritter S, Wadden TA, Sarwer DB (2012) Comparison of bariatric surgical procedures for diabetes remission: efficacy and mechanisms. Diabetes Spectr 25:200–210
12. Frachetti KJ, Goldfine AB (2009) Bariatric surgery for diabetes management. Curr Opin Endocrinol Diabetes Obes 16:119–124
13. Herron DM, Tong W (2009) Role of surgery in management of type 2 diabetes mellitus. Mt Sinai J Med 76:281–293
14. Atkins RC, Zimmet P (2010) Diabetic kidney disease: act now or pay later. Acta Diabetol 47:1–4
15. Tarquini R, Lazzeri C, Pala L, Rotella CM, Gensini GF (2010) The diabetic cardiomyopathy. Acta Diabetol 48:173–181
16. Whiting DR, Guariguata L, Weil C, Shaw J (2011) IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 94:311–321
17. Pories WJ, Swanson MS, MacDonald KG et al (1995) Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. Ann Surg 222:339–350 Discussion 350–332
18. Sjostrom L, Lindroos AK, Peltonen M et al (2004) Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 351:2683–2693
19. Pournaras D, Aasheim E, Sovik T, et al. (2011) A05: Remission of Type 2 diabetes mellitus after bariatric surgery according to the 2009 American Diabetes Association Criteria. 28th Annual Meeting of the American Society for Metabolic and Bariatric Surgery, Orlando, Florida, US, pp 247–248
20. Gagne DJ, Gill G, Urbandt J (2010) P-118: Improvement in Type 1 diabetes after laparoscopic Roux-en-Y gastric bypass. 27th Annual Meeting of the American Society for Metabolic and Bariatric Surgery, Las Vegas, Nevada, US, p S66
21. Lee WJ, Chong K, Ser KH et al (2011) Gastric bypass vs sleeve gastrectomy for type 2 diabetes mellitus: a randomized controlled trial. Arch Surg 146:143–148
22. Boza C, Munoz R, Salinas J et al (2011) Safety and efficacy of Roux-en-Y gastric bypass to treat type 2 diabetes mellitus in non-severely obese patients. Obes Surg 21:1330–1336
23. Reis CE, Alvarez-Leite JI, Bressan J, Alfenas RC (2012) Role of bariatric-metabolic surgery in the treatment of obese type 2 diabetes with body mass index <35 kg/m(2): a literature review. Diabetes Technol Ther 14(4):365–372
24. Hayes MT, Hunt LA, Foo J, Tychinskaya Y, Stubbs RS (2011) A model for predicting the resolution of type 2 diabetes in severely obese subjects following Roux-en Y gastric bypass surgery. Obes Surg 21:910–916
25. Hamza N, Abbas MH, Darwish A, Shafeek Z, New J, Ammori BJ (2011) Predictors of remission of type 2 diabetes mellitus after laparoscopic gastric banding and bypass. Surg Obes Relat Dis 7:691–696
26. Kadera BE, Lum K, Grant J, Pryor AD, Portenier DD, Demaria EJ (2009) Remission of type 2 diabetes after Roux-en-Y gastric bypass is associated with greater weight loss. Surg Obes Relat Dis 5:305–309
27. Lee WJ, Lee YC, Chen JC, Ser KH, Su YH, Chen SC (2010) Preoperative Predictors of Type 2 diabetes resolution after bariatric surgery 27th Annual meeting of the American society for metabolic and bariatric surgery. Surgery for obesity and related diseases. Las Vegas, Nevada, p S23
28. Hall TC, Pellen MG, Sedman PC, Jain PK (2010) Preoperative factors predicting remission of type 2 diabetes mellitus after Roux-en-Y gastric bypass surgery for obesity. Obes Surg 20: 1245–1250
29. Maciejewski ML, Livingston EH, Kahwati LC, Henderson WG, Kavee AL, Arterburn DE (2010) Discontinuation of diabetes and lipid-lowering medications after bariatric surgery at veterans affairs medical centers. Surg Obes Relat Dis 6:601–607
30. Zeni T, Kapur S, Lark TR, Magid P (2009) Diabetes mellitus and insulin resolution after laparoscopic Roux-en-Y gastric bypass. 26th Annual Meeting of the American Society for Metabolic and Bariatric Surgery, Grapevine, Texas, USA, p S43
31. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28:412–419
32. Perugini RA, Shah SA, Kelly JJ, Czerniach DR, Litwin DE, Gallagher-Dorval KA (2009) HOMA estimated glucose disposition index predicts resolution of type 2 diabetes mellitus following laparoscopic gastric bypass 26th Annual Meeting of the American Society for Metabolic and Bariatric Surgery. Surgery for Obesity and Related Diseases, *Grapevine*, Texas, USA, p S1
33. Chikunguwo SM, Wolfe LG, Dodson P et al (2010) Analysis of factors associated with durable remission of diabetes after Roux-en-Y gastric bypass. Surg Obes Relat Dis 6:254–259
34. DiGiorgi M, Rosen DJ, Choi JJ et al (2010) Re-emergence of diabetes after gastric bypass in patients with mid- to long-term follow-up. Surg Obes Relat Dis 6:249–253
35. Deitel M (2009) Slow-progression, autoimmune, type 1 diabetes in adults: a cause of failure of resolution of diabetes after bariatric surgery. Surg Obes Relat Dis 5:705–706
36. Stenstrom G, Gottsater A, Bakhtadze E, Berger B, Sundkvist G (2005) Latent autoimmune diabetes in adults: definition, prevalence, beta-cell function, and treatment. Diabetes 54(Suppl 2): S68–S72