International Journal of Surgery 11 (2013) 309-313

Contents lists available at SciVerse ScienceDirect

# International Journal of Surgery

journal homepage: www.theijs.com

Original research

# Sleeve gastrectomy and Roux-en-Y gastric bypass are equally effective in correcting insulin resistance



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INTERNATION

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# ARTICLE INFO

Article history: Received 10 January 2013 Received in revised form 7 February 2013 Accepted 9 February 2013 Available online 24 February 2013

Keywords: Diabetes mellitus HOMA Insulin resistance Laparoscopic sleeve gastrectomy Laparoscopic Roux-en-Y gastric bypass

# ABSTRACT

*Background:* Laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) are associated with glucose metabolism improvement although data on insulin resistance remission rates after these procedures are lacking.

*Aims:* Primary aim was to compare insulin resistance remission rates achieved after LRYGB and LSG, using population-specific HOMA-IR cut-off points. Secondary objectives were to analyze factors associated with type 2 diabetes mellitus (T2DM) complete remission according to the new American Diabetes Association criteria and to examine changes in HOMA-B during follow-up.

*Methods:* Non-randomized, prospective cohort study of patients undergoing LRYGB or LSG with a minimal follow-up of 24 months. Patients on insulin therapy were excluded.

*Results:* At baseline, 56 (48.7%) of the 115 LRYGB group and 48 (61.5%) of the 78 LSG group had insulin resistance, and 29 (25.2%) and 20 (25.6%) T2DM, respectively. No differences were detected in insulin resistance remission rate (92.9% LRYGB and 87.5% LSG, p = 0.355) nor in T2DM complete remission at 2 years (62.1 vs 60% respectively, p = 0.992). Factors independently associated with T2DM complete remission were diabetes treatment and a greater decrease in 3-month HOMA-IR index. The HOMA-B index showed a progressive decline during follow-up.

*Conclusion:* Both surgical techniques are equally effective in achieving insulin resistance normalization in the majority of severely obese patients. Three-month HOMA-IR reduction after surgery was the main predictor of T2DM complete remission.

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#### 1. Introduction

In addition to weight loss, some bariatric procedures appear to have independent metabolic benefits associated with incretin effects and possibly other hormonal and neural mechanisms.<sup>1</sup> In this respect, laparoscopic sleeve gastrectomy (LSG) has yielded better results than other restrictive techniques in terms of weight loss and improved glucose metabolism<sup>2</sup> but similar or slightly inferior outcomes when compared with hybrid techniques such as laparoscopic Roux-en-Y gastric bypass (LRYGB).<sup>3–5</sup> Although the

beneficial effects of bariatric surgery on glucose metabolism are known, data on insulin resistance remission rates after surgery are lacking. In clinical practice, insulin resistance and beta-cell function have been assessed over the last 20 years by the homeostatic model assessment (HOMA-IR and HOMA-B, respectively).<sup>6</sup> Despite a good correlation with the euglycemic hyperinsulinemic clamp method,<sup>7</sup> the HOMA-IR index varies widely among populations.<sup>8,9</sup> Therefore, specific cut-off points to define insulin resistance in each population should be established.

Given the terminological problems of "remission" versus "cure" and the great heterogeneity among studies in defining remission criteria for type 2 diabetes mellitus (T2DM), the American Diabetes Association (ADA) in 2009 defined and agreed the criteria for partial and complete remission that are stricter than those previously used.<sup>10</sup> Given the short time elapsed, scant studies have evaluated



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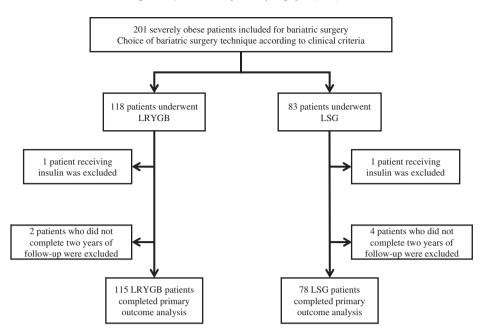


Fig. 1. Study flow diagram. LSG, laparoscopic sleeve gastrectomy; LRYGB, laparoscopic Roux-en-Y gastric bypass. No fatal cases were observed.

the remission rate of T2DM after bariatric surgery in obese diabetic patients with these new criteria. $^5$ 

The primary aim of the present study was to compare insulin resistance remission rates achieved after LRYGB and LSG, using population-specific HOMA-IR cut-off points. Secondary objectives were to examine T2DM complete remission rates after both techniques according to the new ADA criteria and possible associated factors and to study changes in HOMA-B during follow-up.

## 2. Material and methods

# 2.1. Study protocol

A non-randomized, prospective cohort study was conducted on severely obese patients undergoing bariatric surgery at the Hospital del Mar, Barcelona. Patients were aged between 18 and 55 years and met the 1991 bariatric surgery criteria of the National Institutes of Health.<sup>11</sup> Indication for the type of surgical procedure (LRYGB or LSG) was based on clinical criteria and the consensus of the Hospital del Mar Bariatric Surgery Unit. In this respect, LSG was preferred in younger patients, in those with a BMI of 35–40, as a first-step treatment in cases with BMI>50 (although given the positive LSG outcomes none of these patients had to further undergo

#### Table 1

Baseline characteristics of severely obese patients undergoing LRYGB or LSG with a minimum of two years of follow-up.

	LRYGB ( $n = 115$ )	LSG ( <i>n</i> = 78)	p Value
Age (years)	$45.0\pm8.6$	$45.6\pm8.7$	0.640
Gender (% female)	87.8	76.9	0.037
Weight (Kg)	$119.8 \pm 15.8$	$119.3 \pm 17.9$	0.853
Body mass index (Kg/m <sup>2</sup> )	$\textbf{45.8} \pm \textbf{4.3}$	$43.9\pm5.0$	0.006
Waist circumference (cm)	$127.6\pm11.0$	$125.0\pm13.5$	0.394
Fasting glucose (mg/dl)	$110.2\pm26.7$	$111.8 \pm 27.2$	0.691
Insulin (µU/ml)	$14.7\pm8.7$	$17.8 \pm 14.1$	0.066
HOMA-IR	$4.1\pm2.8$	$5.0\pm4.1$	0.075
HOMA-B	$140.4\pm133.1$	$153.5\pm128.1$	0.506
HbA <sub>1c</sub> (%)	$5.6\pm0.8$	$5.7 \pm 0.8$	0.391
Insulin resistance (%)	56 (48.7)	48 (61.5)	0.054
Type 2 diabetes mellitus (%)	29 (25.2)	20 (25.6)	0.539

LRYG, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; HOMA, Homeostatic Model Assesment.

Data presented as mean  $\pm$  standard deviation or percentages. Significance at p < 0.05 was determined using Student's *t*-test for continuous variables and chi-square for categorical variables.

LRYGB), and when drug malabsorption was to be avoided. Patients who did not complete a minimum of 2 year-follow-up were excluded. Because insulinemia is included in the equation for HOMA index calculation, T2DM patients on insulin treatment were also excluded.

Sample size was calculated accepting an alpha risk of 0.05 and a beta risk of 0.20 in a two-sided Student's *t*-test; 65 subjects were required in each group to detect a difference  $\geq$ 1 in the HOMA-IR index as statistically significant. A 3% patient loss rate during follow-up was expected and a 2 standard deviation was assumed.

In accordance with the study protocol approved by the hospital Ethics Committee, all patients were evaluated preoperatively and at 3, 6 and 12 months postsurgery and annually thereafter. Protocol appointments included measurements of weight, waist and hip circumferences, and laboratory tests including glucose, insulin and glycosylated hemoglobin (HbA<sub>1c</sub>) determinations. T2DM pharmacological treatment was recorded at each visit. All patients signed their informed consent for the procedure and for the study.

Two hundred and one patients were operated on between January 2006 and June 2010; of these, 118 underwent LRYGB and 83 LSG. Two diabetic patients (1 of each group) receiving insulin, and 6 patients (2 of the LRYGB group and 4 of the LSG group) who did not complete a minimum of 2 years of follow-up were excluded. Thus, the final analysis included 115 patients undergoing LRYGB and 78 LSG (Fig. 1).

#### 2.2. Anthropometric and biochemical measurements

Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. The percentage of excess weight loss (% EWL) was calculated based on the excess weight above ideal weight (weight corresponding to BMI of 25 kg/m<sup>2</sup>). T2DM diagnosis was defined as two fasting plasma glucose concentrations above 125 mg/dl or HbA<sub>1c</sub>  $\geq$ 6.5% or treatment with oral hypoglycemic agents or insulin.<sup>12</sup>

Glucose was determined by the oxidase method. HbA<sub>1c</sub> was quantified by chromatography (Biosystem, Barcelona, Spain). Insulin was measured by radioimmunoassay (Insulin kit, DPC, Los Angeles, USA). HOMA indexes were estimated using the following formulas<sup>6</sup>: HOMA-IR = insulin ( $\mu$ U/mI) × fasting glucose (mmol/l)/ 22.5 and HOMA-B = 20 × insulin ( $\mu$ U/mI)/[ glucose (mmol/l) – 3.5].

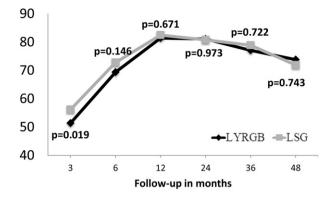
In accordance with data from our population, the cut-off for the HOMA-IR index to define insulin resistance was a level  $\geq$ 3.29.<sup>9</sup> Thus, HOMA <3.29 in patients not using insulin-sensitizing drugs (metformin or glitazones) was established as a criterion of insulin resistance normalization.

T2DM complete remission was defined based on the ADA consensus as a plasma glucose <100 mg/dl with an HbA\_{1c} <6.0% without drug therapy maintained for at least one year.^{10}

# 2.3. Surgical techniques

The LRYGB technique involved a 150-cm antecolic and antegastric Roux limb with 25-mm circular pouch-jejunostomy, with the exclusion of 50 cm of the proximal jejunum. In LSG, the longitudinal resection of the stomach from the angle of His to approximately 5 cm proximal to the pylorus was performed using a 36 French

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**Fig. 2.** Changes in percentage of excess weight loss during follow-up after the bariatric surgical procedure. LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy. Data are expressed as means. Significance at p < 0.05 was determined using Student's *t*-test.

bougie inserted along the lesser curvature. All operations were performed by the same team of surgeons.

#### 2.4. Statistical analysis

Data were expressed as mean  $\pm$  standard deviation for continuous variables and as percentages and frequencies for categorical variables. Student's *t*-test was performed to assess differences between two means. Chi-square or Fisher exact tests were used to evaluate the degree of association of categorical variables. Logistic regression analysis was applied to assess the effects of multiple factors on the T2DM complete remission rate at two years post-bariatric surgery. A *p* value <0.05 was considered statistically significant. Statistical analysis was made with SPSS (version 14.0 for Windows; SPSS, Chicago, IL).

# 3. Results

All 193 patients of the study were Caucasian, with a mean age of  $45.2 \pm 8.7$  years, baseline BMI of  $45.0 \pm 4.7$  kg/m<sup>2</sup> and mean followup of  $2.9 \pm 0.9$  years. Baseline characteristics of LRYGB and LSG patients are listed in Table 1. Patients in the LRYGB group differed from the LSG group in a higher proportion of women and BMI.

Progressive weight loss, more marked during the first 3 months in the LSG group, was observed in both groups during the first year of follow-up. Thereafter, weight loss remained stable and without differences between groups (Fig. 2).

At baseline, 56 (48.7%) patients of the LRYGB group and 48 (61.5%) of the LSG had insulin resistance. Three months after surgery, HOMA-IR had decreased dramatically in both groups (Fig. 3A),

with a remission rate of 91.1% in the LRYGB patients and 91.7% in the LSG, p = 0.914. Insulin resistance remission rate achieved after 2 years of follow-up was 92.9% in LRYB group and 87.5% in LSG (p = 0.355). The HOMA-B index progressively decreased in both groups during follow-up; however, it was significantly higher in the LSG group at the second and third year post-bariatric surgery (Fig. 3B).

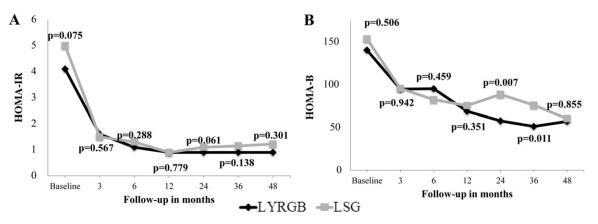
No differences were observed in baseline characteristics of T2DM patients between groups (Table 2). According to the applied bariatric surgery technique, no differences were found in the T2DM complete remission rate (62.1% for LRYGB and 60% for LSG, p = 0.992). Factors independently associated with T2DM complete remission were preoperative diabetes treatment with diet only, compared with oral drug treatment, and a greater decrease in HOMA-IR index values three months post-surgery (Table 3).

# 4. Discussion

The present study showed that two different bariatric surgery techniques, LRYGB and LSG, are equally effective in achieving insulin resistance normalization using a population-specific HOMA-IR cut-off.

Insulin resistance normalization was attained with both surgical techniques in almost all patients as early as 3 months after surgery. This finding suggests that weight loss was not the only factor responsible for the decline in HOMA-IR after bariatric surgery. Previous studies found that surgical techniques with a malabsorptive component like LRYGB produce a greater HOMA-IR reduction than that obtained after restrictive techniques such as vertical banded gastroplasty. Furthermore, this reduction occurred soon after the procedure, when significant weight loss had not yet been achieved.<sup>1</sup> These findings could be explained by changes in gut hormonal mechanisms, such as increased secretion of incretins that enhance insulin sensitivity.<sup>13,14</sup> In the present study, LSG, despite being a restrictive technique, produced an early improvement in insulin sensitivity of a similar magnitude to that achieved with LRYGB. A possible explanation for this finding could be related to the characteristics of the LSG technique. LSG includes a gastric fundus resection, unlike other restrictive techniques, that causes a decrease in ghrelin concentration, a hormone that produces insulin resistance.15-17

In the present study, all patients met the criteria for partial remission and approximately 60% for complete T2DM remission after a 2 year-follow-up. In other studies comparing LRYGB and LSG,



**Fig. 3.** Changes in HOMA during follow-up after the bariatric surgical procedure. A: Changes in HOMA-IR; B: Changes in HOMA-B. HOMA, homeostatic model assessment; HOMA-IR: Model to define insulin resistance, HOMA-B: Model to define beta-cell function; LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy. Data are expressed as means (standard deviation). Significance at p < 0.05 was determined using Student's *t*-test.

#### Table 2

Baseline characteristics of severely obese patients with type 2 diabetes mellitus undergoing LRYG or LSG with a minimum of two years of follow-up.

	LRYGB ( $n = 29$ )	LSG ( $n = 20$ )	p Value
Age (years)	$\overline{49.2\pm6.2}$	50.6 ± 7.4	0.488
Gender (% female)	79.3	75.0	0.492
Body mass index (Kg/m <sup>2</sup> )	$45.7\pm4.6$	$45.6\pm5.8$	0.954
Treatment			
Diet alone (%)	16 (55.2)	7 (35)	0.164
Oral hypoglycemic drugs (%)	13 (44.8)	13 (65)	
Duration of diabetes (years)	$1.3\pm2.4$	$1.5\pm2.5$	0.746
Fasting glucose (mg/dl)	$143.1\pm31.0$	$150.0\pm25.9$	0.415
HbA <sub>1c</sub> (%)	$6.5\pm0.8$	$\textbf{6.9} \pm \textbf{0.7}$	0.113
HOMA-IR	$\textbf{6.1} \pm \textbf{3.3}$	$\textbf{7.6} \pm \textbf{4.8}$	0.212
НОМА-В	$123.0\pm207.6$	$91.3\pm81.9$	0.553

HbA<sub>1c</sub>, glycosylated hemoglobin; HOMA, Homeostatic Model Assesment.

Data presented as mean  $\pm$  standard deviation or percentages. Significance at p < 0.05 was determined using Student's *t* test for continuous variables and Chi-square for categorical variables.

the overall remission rate of T2DM was above 80% with both techniques.<sup>18–24</sup> The lower T2DM remission rate found in the present study could be explained by at least two facts. First, in previous studies there was a wide heterogeneity in the criteria used for diabetes remission. In some studies, remission criteria were non-specified, <sup>19,20,22</sup> others only included diabetes medication withdrawal,<sup>23,24</sup> while others used HbA<sub>1c</sub> <6.5% and fasting glucose <125 mg/dl once medication had been withdrawn.<sup>18,21</sup> And second, in addition to stricter biochemical criteria for T2DM remission (fasting glucose < 100 mg/dl and HbA<sub>1c</sub> < 6.0%), the new ADA criteria require these biochemical parameters to be maintained for at least one year.<sup>10</sup>

In obese patients with short T2DM duration, such as those in our study population, insulin resistance predominates over beta-cell dysfunction.<sup>25</sup> Therefore, in these patients, enhancement of insulin sensitivity is a key factor for glucose metabolism improvement. This is consistent with the finding that HOMA-IR reduction 3 months post-surgery was a predictor of T2DM complete remission two years after the procedure. Moreover, the short duration of diabetes of the subjects included in this study may explain the lack of association of diabetes remission with other factors previously described such as waist circumference and T2DM duration.<sup>26,27</sup>

The HOMA-B index is a marker of pancreatic beta-cell function. In a healthy subject with a normal BMI and no family history of diabetes mellitus, the HOMA-B index is expected to be close to 100, indicating optimal beta-cell function (100%). Subjects in the present study had a mean baseline level above 100 that progressively decreased during follow-up. These results suggest that, preoperatively, beta cells in these patients had a compensatory hyperfunction and, after bariatric surgery, insulin resistance remission caused a decline in this compensatory insulin secretion, reflected in a

## Table 3

Factors related to complete remission of type 2 diabetes mellitus two years after surgery. Odds ratio (OR) obtained by logistic regression analysis.

	OR	95% confidence interval	p Value
Age	0.91	0.78-1.06	0.217
Diet therapy alone	9.69	1.36-69.10	0.023
LRYGB	0.71	0.11-4.77	0.722
Decrease in HOMA-IR units at 3 months	1.31	1.01-1.70	0.045
% EWL at 3 months	1.07	0.99-1.14	0.60

LRYGB, laparoscopic Roux-en-Y gastric bypass; HOMA, Homeostatic Model Assessment; % EWL, percentage excess weight loss.

reduction in the HOMA-B index. On the other hand, surgical techniques with a malabsorptive component cause an increase in hormones with an incretin effect. These hormones raise insulin secretion, but only in the postprandial period. Therefore, the HOMA-B index, which estimates beta-cell function in the fasting state, would not be the optimal method of evaluating postprandial insulin secretion improvement in these patients.<sup>28</sup>

The present study was not without limitations. First, patients were not randomly assigned to either of the bariatric surgery techniques and therefore the baseline characteristics of patients included in each group were not comparable. Second, diabetic patients included in the present study had a short disease duration, the majority did not require pharmacological treatment and those on insulin therapy were excluded. Therefore, the results found cannot be generalized to the whole diabetic population. Finally, insulin resistance was assessed using the HOMA-IR index; however, a more accurate method for quantifying insulin resistance, the euglycemic hyperinsulinemic clamp, was not used since it is invasive and time-consuming.

## 5. Conclusion

In conclusion, LRYGB and LSG are equally effective in achieving insulin resistance normalization in almost all patients. Furthermore, both techniques achieved similar T2DM complete remission rates and HOMA-IR reduction at 3 months after surgery was the main predictor. The HOMA-B index should be carefully interpreted in these patients.

# Ethical approval

Study protocol was approved by the hospital del mar (Barcelona) Ethics Committee.

Funding

None.

# Author contribution

BD contributed for the study design, data collection, data analysis and writing.

FLRJA contributed for the study design and writing.

PBJ contributed for the data analysis and writing.

CJJ contributed for the data analysis and writing.

RM contributed for the data collection.

PA contributed for the data collection.

RJM contributed for the study design.

PM contributed for the study design.

GA contributed for the study design, data analysis and writing.

# Conflict of interest

The authors declare no potential conflicts of interest relevant to this article.

# References

- Rao RS, Yanagisawa R, Kini S. Insulin resistance and bariatric surgery. Obes Rev 2012;13:316–28.
- Abbatini F, Rizzello M, Casella G, Alessandri G, Capoccia D, Leonetti F, et al. Long-term effects of laparoscopic sleeve gastrectomy, gastric bypass, and adjustable gastric banding on type 2 diabetes. Surg Endosc 2009;24:1005–21.
- Lim DM, Taller J, Bertucci W, Riffenburgh RH, O'Leary J, Wisbach G. Comparison of laparoscopic sleeve gastrectomy to laparoscopic Roux-en-Y gastric bypass for morbid obesity in a military institution. *Surg Obes Relat Dis* 2012 [Epub ahead of print].
- Franco JV, Ruiz PA, Palermo M, Gagner M. A review of studies comparing three laparoscopic procedures in bariatric surgery: sleeve gastrectomy, Roux-en-Y gastric bypass and adjustable gastric banding. *Obes Surg* 2011;21:1458–68.
- Schauer PR, Kashyap SR, Wolski K, Brethauer SA, Kirwan JP, Pothier CE, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med 2012;366:1567-76.

# **ORIGINAL RESEARCH**

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- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412–9.
- Levy JC. Evaluation of insulin sensitivity: the HOMA and CIGMA models. Journ Annu Diabetol Hotel Dieu 1998:179–92.
- Haffner SM, Miettinen H, Stern MP. The homeostasis model in the San Antonio Heart study. Diabetes Care 1997;20:1087–92.
- Goday A, Gabriel R, Ascaso JF, Franch J, Ortega R, Martínez O, et al. Cardiovascular risk in subjects with high probability of metabolic syndrome and insulin resistance. *Rev Clin Esp* 2008;208:377–85.
- Buse JB, Caprio S, Cefalu WT, Ceriello A, Del Prato S, Inzucchi SE, et al. How do we define cure of diabetes? *Diabetes Care* 2009;**32**:2133–55.
- Hubbard VS, Hall WH. National Institutes of health consensus development conference draft statement on gastrointestinal surgery for severe obesity. *Obes Surg* 1991;1:257–65.
- Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al., Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 2003;26:3160–7.
- Valverde Y, Puente J, Martín-Duce A, Molina L, Lozano O, Sancho V, et al. Changes in glucagon-like peptide-1 (GLP-1) secretion after biliopancreatic diversion or vertical banded gastroplasty in obese subjects. *Obes Surg* 2005;15: 387–97.
- Laferrere B, Heshka S, Wang K, Khan Y, McGinty J, Teixeira J, et al. Incretin levels and effect are markedly enhanced 1 month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes. *Diabetes Care* 2007;**30**: 1709–16.
- Peterli R, Wölnerhanssen B, Peters T, Devaux N, Kern B, Christoffel-Courtin C. Improvement in glucose metabolism after bariatric surgery: comparison of laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy: a prospective randomized trial. Ann Surg 2009;250:234–41.
- Harvey EJ, Arroyo K, Korner J, Inabnet WB. Hormone changes affecting energy homeostasis after metabolic surgery. Mt Sinai J Med 2010;77:446–65.
- Ramón JM, Salvans S, Crous X, Puig S, Goday A, Benaiges D, et al. Effect of Rouxen-Y gastric bypass vs sleeve gastrectomy on glucose and gut hormones: a prospective randomised trial. J Gastrointest Surg 2012;16:1116–22.

- Abbatini F, Rizzello M, Casella G, Alessandri G, Capoccia D, Leonetti F, et al. Long-term effects of laparoscopic sleeve gastrectomy, gastric bypass, and adjustable gastric banding on type 2 diabetes. Surg Endosc 2010;24:1005–10.
- Kehagias I, Karamanakos SN, Argentou M, Kalfarentzos F. Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy for the management of patients with BMI <50 kg/m<sup>2</sup>. Obes Surg 2011;21:1650–6.
- Lakdawala MA, Muda NH, Goel S, Bhasker A. Single-incision sleeve gastrectomy versus conventional laparoscopic sleeve gastrectomy: a randomised pilot study. Obes Surg 2011;21:1664–70.
- Lee WJ, Chong K, Ser KH, et al. Gastric bypass vs sleeve gastrectomy for type 2 diabetes mellitus: a randomized controlled trial. Arch Surg 2011;146:143-8.
- Leyba JL, Aulestia SN, Llopis SN. Laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy for the treatment of morbid obesity. A prospective study of 117 patients. Obes Surg 2011;21:212–6.
- 23. Nocca D, Guillaume F, Noel P, Picot MC, Aggarwal R, El Kamel M, et al. Impact of laparoscopic sleeve gastrectomy and laparoscopic gastric bypass on HbA1c blood level and pharmacological treatment of type 2 diabetes mellitus in severe or morbidly obese patients. Results of a multicenter prospective study at 1 year. *Obes Surg* 2011;**21**:738–43.
- Bayham BE, Greenway FL, Bellanger DE, O'Neil CE. Early resolution of type 2 diabetes seen after Roux-en-Y gastric bypass and vertical sleeve gastrectomy. *Diabetes Technol Ther* 2012;14:30–4.
- Schinner S, Scherbaum WA, Bornstein SR, Barthel A. Molecular mechanisms of insulin resistance. *Diabet Med* 2005;22:674–82.
  Torquati A, Lutfi R, Abumrad N, Richards WO. Is Roux-en-Y gastric bypass
- Torquati A, Lutfi R, Abumrad N, Richards WO. Is Roux-en-Y gastric bypass surgery the most effective treatment for type 2 diabetes mellitus in morbidly obese patients? J Gastrointest Surg 2005;9:1112–6.
- 27. Schauer PR, Burguera B, Ikramuddin S, Cottam D, Gourash W, Hamad G, et al. Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. *Ann Surg* 2003;**238**:467–84.
- Camastra S, Gastaldelli A, Mari A, Bonuccelli S, Scartabelli G, Frascerra S, et al. Early and longer term effects of gastric bypass surgery on tissue-specific insulin sensitivity and beta cell function in morbidly obese patients with and without type 2 diabetes. *Diabetologia* 2011;54:2093–102.