Predictive factors for diabetes remission after bariatric surgery

Jerry T. Dang, MD
Caroline Sheppard, PhD
David Kim, MD
Noah Switzer, MPH, MD
Xinzhe Shi, MPH, CCRP
Chunhong Tian, PhD
Christopher de Gara, MB, MS
Shahzeer Karmali, MPH, MD
Daniel W. Birch, MSc, MD

Preliminary research was presented at the Society of American Gastrointestinal and Endoscopic Surgeons 2016 Scientific Session and at the 2016 Canadian Surgery Forum.

Accepted Oct. 15, 2018; Early-released Aug. 1, 2019

Correspondence to:
J. Dang
Department of Surgery
University of Alberta Hospital
8440 112 Street NW
Edmonton AB T6G 2B7
dang2@ualberta.ca

DOI: 10.1503/cjs.014516

Background: Bariatric surgery has been shown to induce type 2 diabetes mellitus (T2DM) remission in severely obese patients. After laparoscopic Roux-en-Y gastric bypass (LRYGB), diabetes remission occurs early and independently of weight loss. Previous research has identified preoperative factors for remission, such as duration of diabetes and HbA_{1c}. Understanding factors that predict diabetes remission can help to select patients who will benefit most from bariatric surgery.

Methods: We retrospectively reviewed all T2DM patients who underwent laparoscopic sleeve gastrectomy (LSG) or LRYGB between January 2008 and July 2014. The primary outcome was diabetes remission, defined as the absence of hypoglycemic medications, fasting blood glucose < 7.0 mmol/L and HbA_{1c} < 6.5%. Data were analyzed using multivariable logistic regression analysis to identify predictive factors of diabetes remission.

Results: We included 207 patients in this analysis; 84 (40.6%) had LSG and 123 (59.4%) had LRYGB. Half of the patients (49.8%) achieved diabetes remission at 1 year. Multivariable logistic analysis showed that LRYGB had higher odds of diabetes remission than LSG (odds ratio [OR] 6.58, 95% confidence interval [CI] 2.79–15.50, $p < 0.001$). Shorter duration of diabetes (OR 0.91, 95% CI 0.83–0.99, $p = 0.032$) and the absence of long-acting insulin (OR 0.0011, 95% CI < 0.000–0.236, $p = 0.013$) predicted remission.

Conclusion: Type of bariatric procedure (LRYGB v. LSG), shorter duration of diabetes and the absence of long-acting insulin were independent predictors of diabetes remission after bariatric surgery.

Contexte : Il a été démontré que la chirurgie bariatrique provoque une rémission du diabète de type 2 chez les patients gravement obèses. Après la dérivation gastrique Roux-en-Y (DGRY) par laparoscopie, la rémission du diabète se produit tôt et indépendamment de la perte de poids. Des recherches antérieures ont identifié des facteurs préopératoires de rémission, notamment la durée du diabète et l'HbA_{1c}. Comprendre les facteurs prédictifs de la rémission du diabète peut aider à sélectionner les patients qui bénéficieront le plus de la chirurgie bariatrique.

Méthodes : Nous avons examiné rétrospectivement les dossiers de tous les patients atteints de diabète de type 2 qui ont subi par laparoscopie une gastrectomie en manchon (GM) ou une DGRY entre janvier 2008 et juillet 2014. Le principal résultat a été la rémission du diabète, définie comme l'absence de médicaments hypoglycémiques, la glycémie à jeun < 7,0 mmol/L et l'HbA_{1c} < 6,5 %. Les données ont été soumises à une analyse de régression logistique multiple pour déterminer les facteurs prédictifs de la rémission du diabète.

Résultats : Nous avons inclus 207 patients dans cette analyse; 84 (40,6 %) ont subi une GM et 123 (59,4 %), une DGRY. La moitié des patients (49,8 %) ont obtenu une rémission du diabète à 1 an. L'analyse logistique multiple a montré que la DGRY s'accompagnait de probabilités plus élevées de rémission du diabète que la GM (rapport de cotes [RC] 6,58; intervalle de confiance [IC] de 95 %, 2,79–15,50, $p < 0{,}001$). La durée plus courte du diabète (RC 0,91; IC de 95 %, 0,83–0,99, $p = 0{,}032$) et absence d'insuline à action prolongée (RC 0,0011; IC de 95 % < 0,000–0,236, $p = 0{,}013$) étaient prédicteurs de rémission.

Conclusion : Le type d'intervention bariatrique (DGRY c. MG), la durée plus courte du diabète et l'absence d'insuline à action prolongée étaient des prédicteurs indépendants de la rémission du diabète après une chirurgie bariatrique.

Obesity is a risk factor for the development of type 2 diabetes mellitus (T2DM). Growing evidence supports bariatric surgery as a superior treatment for diabetes in severely obese patients compared with lifestyle modifications or medical management.[1] Bariatric surgery has been shown to improve or induce complete remission of diabetes within a short time frame,[2] even in those with long-standing diabetes.[3] Improvement or remission of diabetes has been observed after all bariatric procedures.[4,5] However, this mechanism is not completely understood, and it is debatable whether weight loss is independent of remission.[4]

Varied response rates of T2DM to surgery have led to several studies looking at predictive factors for diabetes remission. Still and colleagues[6] analyzed a sample of 690 patients with Roux-en-Y gastric bypass and found that insulin use, age, hemoglobin A_{1c} (HbA_{1c}) and hypoglycemic agents were predictive of diabetes remission. Small studies have also found various but similar predictive factors,[4,6–12] in particular that patients with a shorter duration of diabetes and better glycemic control were more likely to experience remission. These predictive factors are similar in long-term studies as well.[13]

The objective of this study was to determine predictive factors for diabetes remission after bariatric surgery at a Canadian tertiary bariatric centre.

Methods

We performed a retrospective chart review of all patients who underwent laparoscopic sleeve gastrectomy (LSG) or laparoscopic Roux-en-Y gastric bypass (LRYGB) at the Royal Alexandra Hospital between January 2008 and July 2014. Inclusion criteria were age ≥ 18 years and preoperative diagnosis of T2DM. Patients were identified as having T2DM based on a previous diagnosis on medical history, or a previous fasting blood glucose > 7.0 mmol/L or HbA_{1c} ≥ 6.5%.[14] Patients with prediabetes, type 1 diabetes mellitus, and incomplete data or follow-up were excluded. This study was approved by the Health Research Ethics Board at the University of Alberta.

In our centre, patients were offered 1 of 3 bariatric procedures: laparoscopic adjustable gastric banding (LAGB), LSG or LRYGB. The decision of which procedure to pursue was made between the patient and the surgeon based on needs and expectations; however, patients with significant reflux were not offered LSG. We did not include LAGB procedures in this study because this procedure was no longer offered to patients after 2014 owing to LAGB being associated with high rates of weight loss failure and long-term complications.[15]

Data collected included demographics, duration of diabetes, smoking and alcohol history, hypertension, and bariatric procedure. Preoperative, postoperative 1 year and postoperative 2 year data were collected on weight, body mass index (BMI), insulin use, hypoglycemic medications and blood test results: fasting blood glucose (FBG), HbA_{1c}, lipid panel, liver transaminases, serum/urine creatinine, and albumin:creatinine ratio.

The primary outcome was diabetes remission, defined as absence of hypoglycemic medications, FBG < 7.0 mmol/L and HbA_{1c} < 6.5%. Glycemic improvement was defined as a decrease in HbA_{1c} of more than 0.5 mmol/L,[16] the use of 1 fewer oral hypoglycemic agent, or discontinued use of short- or long-acting insulin.

Statistical analysis

Statistical analysis was performed using STATA 10 (STATACorp LP) and R 3.2 (The R Foundation) software. Univariate and multivariable logistic regression were completed with STATA to determine independent preoperative factors statistically associated with diabetes remission at 1 year postoperative. A purposeful selection method was used for model building. Any variable with a $p < 0.2$ in univariate analysis was included in multivariable analysis. In the multivariable model, significant variables (Wald test $p < 0.05$) were identified. All important variables that were removed were assessed for confounding effects. If the change in regression coefficients of other variables were over 15%, then the variable would stay in the model. Linear assumption of continuous variables and collinearity were checked. Cook's distance test was used to detect outliers and influential observations in the predictive model. The Hosmer–Lemeshow test was used to test the goodness of fit for the model.

Results

In all, 213 consecutive T2DM patients underwent bariatric surgery between January 2008 and July 2014. Six were excluded because of missing clinical or biochemical data. Of the 207 included patients, 84 (40.6%) had LSG and 123 (59.4%) had LRYGB. The demographic and clinical characteristics of the sample are shown in Table 1, and the average patient preoperative biochemical results are shown in Table 2.

In total, 103 (49.8%) patients achieved diabetes remission at 1 year postoperative. Remission rates were 57.7% and 38.1% for LRYGB and LSG, respectively. Ninety-three (44.9%) patients had 2-year follow-up data. Thirty-five patients who had diabetes remission at 1 year had a 2-year follow-up; 5 (14.3%) of them had diabetes recurrence at 2 years.

Excluding patients who had diabetes remission, 78 (37.7%) patients showed improvement at 1 year postoperative. The total number of patients for all procedures who showed either improvement or remission at 1 year was 181 (87.4%) .

In univariate analysis, patients with diabetes remission were younger ($p = 0.004$), had a shorter duration of diabetes ($p < 0.001$), and used less preoperative insulin ($p < 0.001$) and fewer oral hypoglycemic medications ($p < 0.001$). They also had lower HbA_{1c} ($p < 0.001$), fasting blood glucose ($p = 0.004$), creatinine ($p = 0.018$) and low-density lipoprotein (LDL) ($p = 0.003$). Regarding the

Table 1. Demographic and clinical characteristics and preoperative medications

	Group; mean ± SD or no. (%)		
Characteristic	All patients, *n* = 207	Roux-en-Y gastric bypass, *n* = 123	Sleeve gastrectomy, *n* = 84
Age at surgery, yr	49.7 ± 8.8	49.0 ± 8.5	50.8 ± 9.2
Female sex	153 (73.9)	88 (71.5)	65 (77.4)
Preoperative	46.3 ± 8.1	46.9 ± 7.8	45.4 ± 8.4
Postoperative 1-year BMI, kg/m^2	36.0 ± 7.6	34.6 ± 6.8	38.3 ± 8.3
Preoperative weight, kg	129.3 ± 26.0	131.6 ± 24.8	126.0 ± 27.4
Postoperative 1-year weight, kg	100.6 ± 23.2	97.1 ± 20.8	106.1 ± 25.8
Hypertension	147 (71.0)	90 (73.2)	57 (67.9)
Smoking status			
Ex-smoker	84 (40.6)	52 (42.3)	32 (38.1)
Current smoker	2 (1.0)	1 (0.8)	1 (1.2)
Duration of diabetes, yr	7.6 ± 6.7	8.3 ± 7.0	6.4 ± 6.2
No. of non-insulin diabetes medications	1.5 ± 0.8	1.6 ± 0.9	1.3 ± 0.8
Short-acting insulin	30 (14.5)	20 (16.3)	10 (11.9)
Long-acting insulin	48 (23.2)	32 (26.0)	16 (19.1)

BMI = body mass index; SD = standard deviation.

Table 2. Patient biochemical results

	Timing		
Biochemical result	Preoperative	1 year postoperative	*p* value
HbA_{1c}, %	6.9 ± 1.3	6.1 ± 1.0	< 0.001
Fasting blood glucose, mmol/L	7.4 ± 2.5	6.0 ± 1.7	0.004
LDL, mmol/L	2.1 ± 0.73	2.2 ± 0.8	0.003
HDL, mmol/L	1.1 ± 0.3	1.3 ± 0.3	0.620
Total cholesterol, mmol/L	4.0 ± 1.0	4.1 ± 0.9	0.078
Triglycerides, mmol/L	1.8 ± 1.0	1.4 ± 0.7	0.784
AST, U/L	25.1 ± 12.7	21.0 ± 8.3	0.952
ALT, U/L	33.3 ± 19.6	26.0 ± 14.2	0.476
Serum creatinine, mmol/L	71.2 ± 19.5	65.7 ± 15.8	0.018

ALT = alanine aminotransferase; AST = aspartate aminotransferase; HbA_{1c} = hemoglobin A_{1c}; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

procedure itself, LRYGB was more predictive of remission than LSG ($p = 0.007$; Table 3).

Percent excess weight loss (%EWL) was 51.5 ± 24.7% and percent total weight loss was 22.3 ± 10.0% at 1 year. For LRYGB, %EWL was 59.4 ± 21.6% at 1 year, compared with 38.9 ± 21.1% for LSG. %EWL was not found to be a significant predictor of diabetes remission on univariate analysis ($p = 0.190$) and was not included in the logistic regression model as it is not a preoperative factor.

Multivariable analysis confirmed that LRYGB was associated with higher odds of diabetes remission than LSG (odds ratio [OR] 6.58, 95% confidence interval [CI] 2.79–15.50, $p < 0.001$). Additionally, shorter duration of diabetes (OR 0.91, 95% CI 0.83–0.99, $p = 0.032$) and the absence of long-acting insulin (OR 0.0011, 95% CI < 0.000–0.236, $p = 0.013$) predicted diabetes remission in multivariable analysis after controlling for confounders (sex, hypertension, short-acting insulin, oral hypoglycemic medications, HbA_{1c}, FBG, LDL and creatinine; Table 4).

Table 3. Univariate logistic regression analysis for predictors of diabetes remission

Preoperative factor	*p* value
Age	0.004
LRYGB v. LSG	< 0.001
Sex	0.100
Hypertension	0.052
Duration of diabetes, yr	< 0.001
No. of non-insulin diabetes medications	0.001
Long-acting insulin	< 0.001
Short-acting insulin	< 0.001
Body mass index	0.548
Fasting blood glucose	0.004
HbA_{1c}	< 0.001
LDL	0.003
HDL	0.620
Total cholesterol	0.078
Triglycerides	0.784
AST	0.952
ALT	0.476
Creatinine	0.018

ALT = alanine aminotransferase; AST = aspartate aminotransferase; HbA_{1c} = hemoglobin A_{1c}; HDL = high-density lipoprotein; LDL = low-density lipoprotein; LRYGB = laparoscopic Roux-en-Y gastric bypass; LSG = laparoscopic sleeve gastrectomy.

Table 4. Multivariable logistic regression analysis for predictors of diabetes remission

Preoperative factor	OR (95% CI)*	*p* value
LRYGB vs LSG	6.58 (2.79–15.50)	< 0.001
Duration of diabetes	0.91 (0.83–0.99)	0.032
Preoperative long-acting insulin	0.0011 (0.00–0.24)	0.013

CI = confidence interval; FBG = fasting blood glucose; HbA_{1c} = hemoglobin A_{1c}; LDL = low-density lipoprotein; LRYGB = laparoscopic Roux-en-Y gastric bypass; LSG = laparoscopic sleeve gastrectomy; OR = odds ratio.
*Adjusted for sex, hypertension, short-acting insulin, oral hypoglycemic medications, HbA_{1c}, FBG, LDL and creatinine.

In logistic regression analysis, no variables were forced into the model, and no significant outliers were detected. The Hosmer–Lemeshow test was nonsignificant, indicating the model was a good fit to the data.

Discussion

Type 2 diabetes is estimated to affect 382 million people worldwide and is expected to rise to 592 million by 2035.[17] These patients are at risk for microvascular and macrovascular complications. Medical therapy aims to protect against these complications by achieving tight glycemic control with a target HbA_{1c} < 7.0%.[18] This target can be difficult to achieve for some patients despite aggressive medical therapy. Some have even suggested the use of bariatric surgery for patients with uncontrolled diabetes and a BMI < 35.0 kg/m^2.[19]

Randomized controlled trials have found that bariatric surgery achieved remission in significantly more patients than medical therapy alone.[20–22] Diabetes typically resolved much earlier than weight loss. Different theories attempt to explain the metabolic changes associated with diabetes remission that occur with bariatric surgery.[23] The hindgut hypothesis postulates that rapid delivery of nutrients to the distal intestine enhances release of hormones such as glucagon-like peptide-1.[23] On the other hand, the foregut hypothesis suggests that bypassing the proximal intestine reduces secretion of anti-incretin hormones.[23] Both of these effects lead to early improvement of glucose metabolism.[23]

Consistent with our results, previous studies have shown that diabetes remission occurs most often with LRYGB compared with LSG.[20,24] The etiology behind diabetes remission after LSG is thought to be primarily weight dependent, unlike LRYGB which is weight-independent as remission occurs before any significant weight loss. However, animal studies point to changes in bile acids and resultant changes in the gut microbiome as the reason for improved glucose homeostasis.[25] Further studies will be needed to clarify the physiology behind diabetes remission after LRYGB and LSG. The predictive factors we found in our analysis included shorter duration of diabetes and the absence of long-acting insulin use. This is consistent with multiple previous studies analyzing predictive factors of diabetes remission.[4,6–12] However, some of the studies found that other factors, such as age, C-peptide, BMI, HbA_{1c}, FBG, hypertension and waist circumference, were also predictive.[4,6–12] In general, our results and those of previous studies suggest that a shorter duration of diabetes and better diabetes control are predictors of remission. A longer duration of disease reduces b-cell function, resulting in worsened diabetes control.[26] Age ties into this, as older patients tend to have had a longer duration of diabetes. This suggests that earlier bariatric surgery in patients with diabetes may be more effective in improving diabetic outcomes.

Aminian and colleagues[27] developed a scoring system that divided diabetes severity into 3 stages and compared rates of diabetes remission between LRYGB and LSG. Patients with mild diabetes had similar diabetes remission after LRYGB and LSG, whereas patients in the moderate category had significantly higher rates of diabetes remission after LRYGB (60% v. 25%). In the severe category, the rate of diabetes remission was low in both groups. Patients in this group likely have poor functional b-cell reserve, and earlier surgical intervention may have been more effective. Furthermore, this study demonstrates that LRYGB does not always have better remission that LSG, and likely depends on the severity of disease.

Diabetes remission may not persist in some patients. Our study, despite limited 2-year follow-up data, had a 14.3% diabetes recurrence rate after diabetes remission. Schauer and colleagues[28] defined glycemic relapse as patients who had an HbA_{1c} ≤ 6.0% at 1 year but not at 3 years, and they found a glycemic relapse rate of 24% in the LRYGB cohort and 50% in the LSG cohort. However, despite glycemic relapse, patients continued to show improved glycemic control and required fewer diabetes medications overall at 3 years compared with baseline.

Limitations

Limitations of our study were primarily associated with its retrospective nature. Waist circumference was missing from the majority of patient records, and this factor could not be incorporated into our model. Another limitation is that only 44.9% of patients had 2-year follow-up data. There were 5 patients who had recurrence of diabetes after remission, and it is not known if more patients will experience recurrence as time from surgery increases. Future studies with data beyond 2 years are needed to create stronger clinical tools and models for predicting long-term diabetes remission.

Another limitation of our study is that weight loss after LSG was lower than reported in the literature. This is likely because of the standardized use of a 50-Fr bougie at our centre. We have chosen this size because a recent systematic review reported that a bougie size greater than 40-Fr had a lower risk of leak.[29] This study also showed that bougie size < 40-Fr was associated with more rapid weight loss at 6 months than bougie size > 40-Fr; however, both groups ended up with similar weight loss at 36 months. Canada has a publicly funded health system with scarce resources, where less than 0.1% of patients who are eligible for publicly funded bariatric surgery actually receive it.[30]

Conclusion

Diabetes remission occurred in 49.8% of patients by 1 year post–bariatric surgery. Our study also provides further evidence that patients who have diabetes should undergo LRYGB instead of LSG. The type of bariatric procedure, shorter duration of diabetes and the absence of long-acting insulin were independent predictors of remission. Understanding factors that are predictive of diabetes remission can help triage diabetic patients to those who will benefit most from bariatric surgery. Future studies should be directed at understanding the physiology of diabetes improvement and remission after LRYGB and LSG.

Affiliations: From the Department of Surgery, University of Alberta, Edmonton, Alta. (Dang, Switzer); the Department of Surgery, University of British Columbia, Vancouver, BC (Kim); and the Centre for the Advancement of Minimally Invasive Surgery (CAMIS), Royal Alexandra Hospital, Edmonton, Alta. (Sheppard, Shi, Tian, Karmali, Birch).

Competing interests: S. Karmali is a consultant for Gore Medical and Ethicon. D. Birch is a consultant and has received educational grants from Ethicon and Covidien, educational grants from Stryker, and teaching honoraria from Cook Surgery and Bard Davol. No other competing interests declared.

Contributors: J. Dang, C. Sheppard, C. Tian, C. de Gara, S. Karmali and D. Birch designed the study. J. Dang and D. Kim acquired the data, which J. Dang, C. Sheppard, N. Switzer, X. Shi, and C. Tian analyzed. J. Dang and C. Sheppard wrote the article, which all authors reviewed and approved for publication.

References

1. Courcoulas AP, Belle SH, Neiberg RH, et al. Three-year outcomes of bariatric surgery vs lifestyle intervention for type 2 diabetes mellitus treatment. *JAMA Surg* 2015;150:931-40.
2. Ardestani A, Rhoads D, Tavakkoli A. Insulin cessation and diabetes remission after bariatric surgery in adults with insulin-treated type 2 diabetes. *Diabetes Care* 2015;38:659-64.
3. Casella G, Abbatini F, Cal B, et al. Ten-year duration of type 2 diabetes as prognostic factor for remission after sleeve gastrectomy. *Surg Obes Relat Dis* 2011;7:697-702.
4. Panunzi S, De Gaetano A, Carnicelli A, et al. Predictors of remission of diabetes mellitus in severely obese individuals undergoing bariatric surgery. *Ann Surg* 2015;261:459-67.
5. Edelman S, Ng-Mak DS, Fusco M, et al. Control of type 2 diabetes after 1 year of laparoscopic adjustable gastric banding in the helping evaluate reduction in obesity (HERO) study. *Diabetes Obes Metab* 2014;16:1009-15.
6. Still CD, Wood GC, Benotti P, et al. Preoperative prediction of type 2 diabetes remission after Roux-en-Y gastric bypass surgery: a retrospective cohort study. *Lancet Diabetes Endocrinol* 2014;2:38-45.
7. Blackstone R, Bunt JC, Cortés MC, et al. Type 2 diabetes after gastric bypass: remission in five models using HbA1c, fasting blood glucose, and medication status. *Surg Obes Relat Dis* 2012;8:548-55.
8. Dixon JB, Chuang L-M, Chong K, et al. Predicting the glycemic response to gastric bypass surgery in patients with type 2 diabetes. *Diabetes Care* 2013;36:20-6.
9. Hall TC, Pellen MGC, Sedman PC, et al. Preoperative factors predicting remission of type 2 diabetes mellitus after Roux-en-Y gastric bypass surgery for obesity. *Obes Surg* 2010;20:1245-50.
10. Hayes MT, Hunt LA, Foo J, et al. A model for predicting the resolution of type 2 diabetes in severely obese subjects following Roux-en Y gastric bypass surgery. *Obes Surg* 2011;21:910-6.
11. Lee WJ, Chong K, Chen JC, et al. Predictors of diabetes remission after bariatric surgery in Asia. *Asian J Surg* 2012;35:67-73.
12. Robert M, Ferrand-Gaillard C, Disse E, et al. Predictive factors of type 2 diabetes remission 1 year after bariatric surgery: impact of surgical techniques. *Obes Surg* 2013;23:770-5.
13. Arterburn DE, Bogart A, Sherwood NE, et al. A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. *Obes Surg* 2013;23:93-102.
14. Canadian Diabetes Association. Diabetes: clinical practice guidelines. *Can J Diabetes* 2013;37:212.
15. DeMaria EJ, Sugerman HJ, Meador JG, et al. High failure rate after laparoscopic adjustable silicone gastric banding for treatment of morbid obesity. *Ann Surg* 2001;233:809-18.
16. Karyekar CS, Frederich R, Ravichandran S. Clinically relevant reductions in HbA 1c without hypoglycaemia: results across four studies of saxagliptin. *Int J Clin Pract* 2013;67:759-67.
17. Guariguata L, Whiting DR, Hambleton I, et al. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract* 2014;103:137-49.
18. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977-86.
19. Rubino F, Kaplan LM, Schauer PR, et al. The Diabetes Surgery Summit Consensus Conference. *Ann Surg* 2010;251:399-405.
20. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med* 2012;366:1567-76.
21. Ikramuddin S, Korner J, Lee W-J, et al. Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia. *JAMA* 2013;309:2240–9.
22. Mingrone, G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med* 2012;366:1577-85.
23. Mingrone G, Castagneto-Gissey L. Mechanisms of early improvement / resolution of type 2 diabetes after bariatric surgery. *Diabetes Metab* 2009;35(6 PART II):518-23.
24. Pournaras DJ, Osborne A, Hawkins SC, et al. Remission of type 2 diabetes after gastric bypass and banding: mechanisms and 2 year outcomes. *Ann Surg* 2010;252:966-71.
25. Ryan KK, Tremaroli V, Clemmensen C, et al. FXR is a molecular target for the effects of vertical sleeve gastrectomy. *Nature* 2014;509:183-8.
26. Madsbad S, Faber O, Binder C, et al. Prevalence of residual beta-cell function in insulin-dependent diabetics in relation to age at onset and duration of diabetes. *Diabetes* 1978;27:262-4.
27. Aminian A, Brethauer SA, Andalib A, et al. Individualized metabolic surgery score: procedure selection based on diabetes severity. *Ann Surg* 2017;266:650-7.
28. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes — 3-year outcomes. *N Engl J Med* 2014;370:2002-13.
29. Parikh M, Issa R, McCrillis A, et al. Surgical strategies that may decrease leak after laparoscopic sleeve gastrectomy: A systematic review and meta-analysis of 9991 cases. *Ann Surg* 2013;257:231-7.
30. Padwal RS, Chang H-J, Klarenbach S, et al. Characteristics of the population eligible for and receiving publicly funded bariatric surgery in Canada. *Int J Equity Health* 2012;11:54.