Systematic review of risk prediction models for diabetes after bariatric surgery

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Background: Diabetes remission is an important outcome after bariatric surgery. The purpose of this study was to identify risk prediction models of diabetes remission after bariatric surgery.

Methods: A systematic literature review was performed in MEDLINE, MEDLINE-In-Process, Embase and the Cochrane Central Register of Controlled Trials databases in April 2015. All English-language full-text published derivation and validation studies for risk prediction models on diabetic outcomes after bariatric surgery were included. Data extraction included population, outcomes, variables, intervention, model discrimination and calibration.

Results: Of 2330 studies retrieved, eight met the inclusion criteria. Of these, six presented development of risk prediction models and two reported validation of existing models. All included models were developed to predict diabetes remission. Internal validation using tenfold validation was reported for one model. Two models (ABCD score and DiaRem score) had external validation using independent patient cohorts with diabetes remission assessed at 12 and 14 months respectively. Of the 11 cohorts included in the eight studies, calibration was not reported in any cohort, and discrimination was reported in two.

Conclusion: A variety of models are available for predicting risk of diabetes following bariatric surgery, but only two have undergone external validation.

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Introduction

The prevalence of obesity (BMI 30 kg/m² or more) has been increasing worldwide1,2. Bariatric surgery is the most effective treatment for morbid obesity3, resulting in a significant decrease in weight, as well as amelioration of associated co-morbidities including type 2 diabetes mellitus (T2DM)4–6, cardiovascular diseases7, obstructive sleep apnoea8 and musculoskeletal disorders9. A decrease in the number of co-morbidities may lead to a reduction in the healthcare resources associated with managing severe and complex obesity10–12.

Risk prediction models are based either on approximations of absolute probability or on the risk that a specific outcome can occur within a certain time period in a subject with an individual predictor profile (through the use of predictor variables (co-variables))13. Risk predictors include patient characteristics (such as age and sex), medical history, blood chemistry results and genetic markers. Predictors for diabetes resolution include the mode of diabetes control (diet, oral hypoglycaemic drugs, insulin), good glycaemic control, age at surgery, duration of diabetes and waist circumference14,15.

Development of a multivariable prediction model requires a number of steps: selecting a set of candidate predictors; identifying important predictors among them by regression analysis; specifying a model by assigning relative weights for each predictor in a combined risk calculator; estimating performance of the model by measuring model calibration and discrimination; and conducting internal validation to assess the potential for optimism and adjusting the model for overfitting when necessary13. Good models are usually derived from large observational studies.
Risk prediction models are used to guide clinicians and patients in a joint decision-making process for selection of appropriate treatments. Accurate prognostic assessment may safeguard against putting patients in a high-risk situation, which in turn could prevent an unnecessary economic burden on healthcare systems. To achieve this, prognostic models must be accurate and generalizable. Internal validation is not sufficient to confirm that a model that successfully predicts the outcome of interest is valuable or applicable to new individuals. Thus, external validation of any such model in new individuals is very important.

Calibration and discrimination are major evaluation methods for prediction models. Calibration refers to the agreement between observed and predicted outcomes. It can be assessed graphically by plotting, or statistically by testing for goodness of fit. Discrimination refers to the ability to discriminate individuals with the outcome from those without it. Statistics commonly used to evaluate discrimination performance of prediction models include the concordance (or c) statistic, or area under the ROC curve (AUC). Thus, external validation is not sufficient to confirm that a model that successfully predicts the outcome of interest is valuable or applicable to new individuals.

The objective of this systematic review was to identify studies that have developed or validated risk prediction models for remission of T2DM after bariatric surgery and describe their performance.

Methods

Literature search and citation screening

A systematic literature search was performed in MEDLINE, MEDLINE-In-Process, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL). A detailed description of the search strategy used in each database, and the selection process as adapted from the PRISMA framework, is presented in Appendix S1. Searches were conducted on 28 April 2015, and were restricted to full-text articles. There was no restriction on the timespan of the search.

Abstract screening was carried out by two reviewers. The evaluation of full-text publications was performed by a single reviewer using the inclusion and exclusion criteria provided below. A second reviewer checked the appropriateness of inclusion of studies. Disagreements were resolved by consensus.

Study selection

Studies were considered for inclusion based on the following criteria: intervention (bariatric surgery); type of study (observational studies, randomised controlled trials); predictive model (at least two risk factors or validation studies); outcomes reported (diabetes outcomes); and language (English). Validation studies were included when the study validated the model in relation to the same outcome as reported in the derivation study.

Data extraction and analysis

The following data from each included publication were extracted by one reviewer: population characteristics; intervention; selection of variables; number of subjects in the derivation and/or validation cohorts; source of the study population; internal validation; model calibration; and discrimination.

Assessment of model performance

Data related to discrimination (the ability of a model to recognize individuals who experience the outcome from those who do not) and calibration (agreement between the model estimated outcome and the observed outcome) were abstracted. Discrimination is typically identified from the c-statistic, or area under the ROC curve (AUC). An AUC of 0.500 suggested no discriminatory power, 0.501–0.699 poor discriminatory power, 0.700 to 0.799 acceptable discriminatory power, 0.800–0.899 excellent discriminatory power, and 0.900 to 1 indicated outstanding discriminatory power. Model calibration is commonly identified with Hosmer–Lemeshow tests or correlation coefficients.

Results

The search strategy yielded 2330 citations. Of these, 102 studies were eligible for full-text review and eight studies, evaluating six risk prediction models, were selected (Fig. 1). Articles excluded with reasons for exclusion are shown in Table S1 (supporting information). All models focused on prediction of remission of T2DM. Among the six published risk prediction models, two were validated in one or more independent cohorts. Among the remaining four models, one was internally validated (by 10-fold validation method), whereas the remaining models were not validated. Table 1 summarizes the characteristics of the included studies. Models were developed and validated in cohorts varying widely in patient sample size, with a median of 103 (range 46–690) patients.
Risk prediction models for diabetes after bariatric surgery

**ABCD score**

The ABCD score includes four categorical variables to predict remission of T2DM: BMI, C-peptide, T2DM duration and age. The ABCD score ranges from 0 to 10 points by summing the points for each variable, with high scores indicating a greater chance of remission. The ABCD score was derived from a multicentre cohort including 63 patients who had a BMI of at least 35 kg/m², or a BMI below 35 kg/m² but with poorly controlled T2DM, and who had undergone laparoscopic gastric bypass for uncontrolled T2DM. Patient follow-up in the derivation cohort was at least 3 years. Internal validation was not performed in the derivation cohort.

The model has been validated in three independent cohorts, including a total of 341 patients who underwent bariatric surgery, using the outcome T2DM remission at 1 year after surgery. The validation cohorts were mainly from the same institutions as the derivation cohort, but at a later time. Three cohorts consisted of patients with a mean age ranging from 42 to 48 years, 48–63 per cent women, a BMI between 26.9 and 39.0 kg/m², and a T2DM duration ranging from 2.4 to 6.5 years before the surgery. Patients underwent either laparoscopic gastric bypass (Roux-en-Y gastric bypass, LYGB) or laparoscopic sleeve gastrectomy.

Model calibration or discrimination was not reported in either the derivation or validation cohorts.

**DiaRem score**

The DiaRem score was developed to predict remission of T2DM after RYG. It includes four variables. Three of these are categorical (age, glycosylated haemoglobin A1c (HbA1c) level and other diabetes drug groups) and a single binomial variable: treatment with insulin. The DiaRem score ranges from 0 to 22, with low scores predicting a high probability of remission and high scores the converse. The DiaRem score was derived from a retrospective cohort of 690 patients with T2DM with at least 14 months of follow-up. Internal validation was not performed in the derivation cohort.

The model has been validated in two independent single-centre cohorts of 389 patients in total undergoing RYG at 14 months after the surgery. These cohorts involved patients with a mean BMI of 48.4 and 49.5 kg/m², a female prevalence of 68 and 74 per cent, and a mean insulin use of 28 and 38 per cent in each cohort. All patients underwent RYG surgery.

Model calibration or discrimination was not reported in either the derivation or validation cohorts.

**Risk prediction models without validation in independent cohorts**

There were four models without external cohort validation. Dixon and colleagues developed a risk calculator that estimates the likelihood of an individual achieving remission of T2DM. The model includes two continuous variables: BMI and diabetes duration. The derivation cohort evaluated in a prospective longitudinal study included 103 patients who underwent laparoscopic gastric bypass with a follow-up of 12 months. Internal validation was not performed. Discrimination was assessed with a ROC curve. Optimal cut-off points of BMI exceeding 27 kg/m² or a duration of diabetes shorter than 7 years, provided sensitivities, specificities and AUC values of 68 per cent, 71 per cent and 0.69; and 69 per cent, 63 per cent and 0.66, respectively.

Hayes and co-workers published a risk calculator for remission of T2DM with two variables. The model includes one binominal variable (diabetes status) and one continuous variable (preoperative HbA1c). The derivation cohort was evaluated in a prospective single-centre study.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Derivation/ validation</th>
<th>Data collection</th>
<th>Model description</th>
<th>Population*</th>
<th>Model evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al.²³</td>
<td>Derivation</td>
<td>n.r.</td>
<td>ABCD score: age, BMI, C-peptide, and T2DM duration (Remission of T2DM at 12 months)</td>
<td>63 patients undergoing LGB Age 38-4 years, 76% female, BMI 39-1 kg/m², T2DM duration 2-6 years Follow-up ≥ 3 years</td>
<td>n.r. n.r. n.r.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Validation</td>
<td>Prospective</td>
</tr>
<tr>
<td>Lee et al.²⁹</td>
<td>Validation</td>
<td>n.r.</td>
<td>ABCD score</td>
<td>80 patients undergoing LGB or LSG Age 47-7 years, 63% female, BMI 26-9 kg/m², T2DM duration 6-5 years Follow-up 12 months</td>
<td>n.a. n.r. n.r.</td>
</tr>
<tr>
<td>Lee et al.³⁰</td>
<td>Validation Retrospective</td>
<td>n.r.</td>
<td>ABCD score</td>
<td>85 patients undergoing LSG Age 41-9 years, 48% female, BMI 39-0 kg/m², T2DM duration 2-7 years Follow-up 12 months</td>
<td>n.a. n.r. n.r.</td>
</tr>
<tr>
<td>Still et al.²⁴</td>
<td>Derivation Retrospective</td>
<td>n.r.</td>
<td>DiaRem score: age, HbA1c, other diabetes drugs, and treatment with insulin (Remission of T2DM at 14 months)</td>
<td>690 patients undergoing RYGB Age 51-2 years, 73% female, BMI 49-4 kg/m², insulin use 36% Follow-up ≥ 14 months</td>
<td>n.r. n.r. n.r.</td>
</tr>
<tr>
<td>Validation (in Scottsdale cohort)</td>
<td>n.r.</td>
<td>DiaRem score</td>
<td></td>
<td>276 patients undergoing RYGB 68% female, BMI 48-4 kg/m², insulin use 28% Follow-up 14 months</td>
<td>n.a. n.r. n.r.</td>
</tr>
<tr>
<td>Validation (in Danville cohort)</td>
<td>n.r.</td>
<td>DiaRem score</td>
<td></td>
<td>113 patients undergoing RYGB 74% female, BMI 49-5 kg/m², insulin use 38% Follow-up 14 months</td>
<td>n.a. n.r. n.r.</td>
</tr>
<tr>
<td>Dixon et al.²⁶</td>
<td>Derivation Prospective</td>
<td></td>
<td>BMI, and diabetes duration (Remission of T2DM at 12 months)</td>
<td>103 patients undergoing LGB Age 47-5 years, 60% female, BMI ≤ 30 (mean 26) kg/m², T2DM duration 8-2 years Follow-up 12 months</td>
<td>n.r. n.r. n.r.</td>
</tr>
</tbody>
</table>

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Table 1 Continued

<table>
<thead>
<tr>
<th>Reference</th>
<th>Derivation/validation</th>
<th>Data collection</th>
<th>Model description</th>
<th>Population*</th>
<th>Internal validation</th>
<th>Calibration</th>
<th>Discrimination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hayes et al.25</td>
<td>Derivation Prospective</td>
<td>Use of insulin versus other drugs and preoperative HbA1c (Remission of T2DM at 12 months)</td>
<td>127 patients undergoing gastric bypass Age 48 ± 5 years, 65% female, mean BMI 46.8 kg/m², diabetes duration 4 ± 5 years Follow-up 12 months</td>
<td>Yes (tenfold) n.r. n.r.</td>
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<tr>
<td>Robert et al.28</td>
<td>Derivation Retrospective</td>
<td>BMI ≤ 50 kg/m², Diabetes duration ≤ 4 years, HbA1c ≤ 7.1%, Fasting glucose ≤ 114 mg/dl, Oral anti-diabetic agent treatment without insulin (Remission of T2DM at 12 months)</td>
<td>46 patients undergoing LAGB, LRYGB or LSG Age 45 ± 3 years, 68% female, BMI 49.5 kg/m², diabetes duration 3 ± 0 years Follow-up 12 months</td>
<td>n.r. n.r. AUC 0.950 (95 per cent c.i. 0.838 to 0.992; P &lt; 0.001)</td>
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<tr>
<td>Ugale et al.27</td>
<td>Derivation Retrospective</td>
<td>Diabetes remission score Age, BMI, T2DM duration, Microvascular complications, Macrovascular complications, Preoperative insulin use, and Stimulated C-peptide Remission of T2DM at 12 months</td>
<td>75 patients undergoing IISG or IIDSG Age 54 ± 0 years, 35% female, BMI 24.3 kg/m², T2DM duration 10 ± 0 years Mean follow-up 30 ± 2 months (IISG), 12 ± 7 months (IIDSG)</td>
<td>n.r. n.r. n.r.</td>
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</table>

*Age, BMI, type 2 diabetes mellitus (T2DM) duration reported as mean values unless otherwise specified. n.r., Not reported; LGB, laparoscopic gastric bypass; n.a., not applicable; LSG, laparoscopic sleeve gastrectomy; HbA1c, glycated haemoglobin; (L)RYGB, (laparoscopic) Roux-en-Y gastric bypass; AUC, area under receiver operating characteristic (ROC) curve; LAGB, laparoscopic adjustable gastric banding; IISG, ileal interposition coupled sleeve gastrectomy; IIDSG, ileal interposition diverted sleeve gastrectomy.

of 127 patients with T2DM who underwent gastric bypass. Follow-up of the derivation cohort was 12 months. Internal validation was conducted using the tenfold cross-validation method. Calibration or discrimination statistics were not evaluated.

Robert et al.28 published a risk prediction score for remission of T2DM with five variables. The model was based on a retrospective cohort of 46 patients with T2DM, who had a BMI of 35 kg/m² or more with follow-up of 12 months. The risk prediction score ranges from 0 to 5 with five binomial variables (Table 1). Discrimination was assessed by ROC analysis; the AUC was 0.950 (95 per cent c.i. 0.838 to 0.992; P < 0.001), indicating outstanding discriminatory power. A cut-off value in the risk prediction score of 2 or more provided 97 per cent sensitivity in predicting diabetes remission, with 86 per cent specificity.

Ugale and colleagues27 proposed a scoring system with seven variables for postoperative diabetes remission. The scoring system was derived from a retrospective cohort of 75 patients with poorly controlled T2DM who underwent the experimental method of ileal interposition in combination with two varieties of sleeve gastrectomy. The mean follow-up was 30 ± 2 and 12 ± 7 months for two groups with different types of sleeve gastrectomy. Internal validation, calibration and discrimination were not reported.

Discussion

This systematic review identified and evaluated six risk prediction models for diabetes outcomes after bariatric surgery. Only two models (ABCD score23 and DiaRem
The surgery types were mainly gastric bypass and sleeve gastrectomy. The ABCD score was developed from a cohort of patients who underwent gastric bypass\(^{23}\). It was validated in two cohorts: one with gastric bypass and the other including both bypass and sleeve gastrectomy\(^{29,10}\). The DiaRem score was developed and validated in patients undergoing RYGB\(^{24}\). A systematic review\(^{33}\) that compared the co-morbidity outcomes after laparoscopic RYGB and sleeve gastrectomy showed that RYGB and sleeve gastrectomy had similar effects on T2DM. Only the model of Robert and colleagues\(^{28}\) included a mixture of all current treatment options. The diabetes remission model proposed by Ugale et al.\(^{27}\) utilized modifications of sleeve gastrectomy.

The geographical origin of the derivation cohorts might also be important for understanding the value of the developed models. The ABCD score\(^{23}\), the diabetes remission score\(^{27}\) and the model of Dixon et al.\(^{26}\) were developed in Asian populations. The DiaRem score was based on a cohort in the USA\(^{24}\), and the model reported by Hayes and colleagues\(^{25}\) was developed in New Zealand. The only model developed in a European cohort is that by Robert and co-workers\(^{28}\).

Output format can also be important for ease of use of models in clinical practice. The ABCD score\(^{23}\), the DiaRem score\(^{24}\), the diabetes remission score proposed by Ugale and colleagues\(^{27}\) and the algorithm proposed by Robert et al.\(^{28}\) are risk scores. Therefore, the various model estimates are translated to a particular number of points along a scale of increasing risk, which in turn correspond to a certain probability of remission. Scores might be less intuitive than risks or chances of remission, and may require extensive use to allow easy day-to-day interpretation of the results in relation to an individual patient’s prognosis. Hayes and colleagues\(^{25}\) proposed two formulas to determine whether a patient is likely to recover from diabetes if the value in one formula (‘class resolved’) is higher than that in the other (‘class not resolved’). Dixon and co-workers\(^{26}\) proposed a simple formula to calculate the likelihood of remission.

All published risk prediction models have limitations in quality and further validation is required. They still might be of relevance for clinical practice. The type of surgery, patient population, output format, and availability of inputs to physician and patients can all influence the choice of model. Limitations of each model need to be evaluated, acknowledged and considered before implementation into clinical practice. The optimal management of bariatric surgery requires accurate assessment of prognosis, and this is still challenging.
Acknowledgements

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Disclosure: The authors declare no other conflict of interest.

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24 Still CD, Wood GC, Benotti P, Petrick AT, Gabrielsen J, Strodel WE et al. Preoperative prediction of type 2 diabetes...


Supporting information

Additional supporting information may be found in the online version of this article:

Appendix S1 Search strategies (Word document)
Table S1 Publications excluded after review of full text (Word document)