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Role of DiaRem Score in Preoperative Prediction of Type 2 Diabetes Mellitus Remission After Laparoscopic Roux-en-Y Gastric Bypass: Indian Perspective

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Abstract

Background Roux-en-Y gastric bypass (RYGB) has emerged as the most effective treatment in reversing insulin resistance in patients with type 2 diabetes mellitus (T2DM). A number of models and statistical tools have been proposed to predict patients likely to experience diabetes remission post-RYGB. The purpose of our study was to evaluate the preoperative accuracy of DiaRem score in predicting T2DM remission at 1 year of follow-up in a retrospective analysis of diabetic morbidly obese patients who underwent RYGB.

Methods One hundred and forty-three patients underwent RYGB between January 2018 and December 2018. We conducted a retrospective analysis in 55 patients (38.46%) with T2DM with 1 year of follow-up. DiaRem score was calculated, and patients were stratified in five groups.

Result At a 1-year follow-up, we found a higher proportion of patients with T2DM remission in the lower score group compared to a lower proportion of patients with remission in the higher score group. We derived a DiaRem cut-off score of 6.5 that had high sensitivity and specificity to predict T2DM remission preoperatively. We found a significant decrease in BMI and HbA1C values post-operatively at 1 year following RYGB.

Conclusion DiaRem score is an easy to determine score based on basic clinical parameters that could identify patients with T2DM who would achieve maximal benefit in terms of remission after bariatric surgery. The development of a suitable scoring tool would be clinically useful as it would enable clinicians to better triage patients for RYGB.

Keywords DiaRem score · Roux-en-Y gastric bypass · Type 2 DM remission

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Introduction

Bariatric surgery has emerged as the most effective treatment in reversing insulin resistance in patients with type 2 diabetes [1]. Roux-en-Y gastric bypass (RYGB) surgery, most commonly performed in patients with a BMI of 35 kg/m^2 or greater, is a particularly effective intervention, with about 60% of patients achieving remission of type 2 diabetes [2, 3]. RYGB surgery has also been proposed as a way to achieve remission of type 2 diabetes in individuals for whom the primary objective might not be weight loss, such as those with a BMI of $25\text{--}35 \text{ kg/m}^2$ [4, 5]. However, recent work suggests that preoperative clinical (e.g. age, BMI, duration of diabetes) and biological markers (e.g. HbA1C, C-peptide) predict responsiveness to RYGB for weight loss and diabetes remission [6, 7]. This suggests that

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not all people derive equal benefit from bariatric surgery and better assessment tools are needed prior to surgery to understand who is likely to meet T2DM remission criteria and obtain the best results.

A number of models and statistical tools have been utilized to predict which patients would experience diabetes remission post-RYGB; however, clinical applicability and relevance have been questioned. The development of a suitable scoring tool would be clinically useful as it would enable clinicians to better triage patients for RYGB. More recently, the DiaRem score, proposed by Still et al., demonstrated the best performance characteristics and ease of use in the clinical setting. Of 259 initial preoperative clinical variables explored, 4 were found to be independent predictors of diabetes remission following RYGB: age, haemoglobin A1C (HbA1C) or glycosylated Hb, use of a sulfonylureas and an insulin-sensitizing agent (ISA) and treatment with insulin [8].

The purpose of our study was to evaluate the preoperative accuracy of DiaRem score in predicting T2DM remission at 1 year of follow-up of diabetic morbidly obese patients who underwent RYGB in our high volume bariatric centre. The primary objectives were as follows:

- To evaluate the preoperative predictive ability of DiaRem score at a 1-year follow-up post-RYGB
- To determine the efficacy of RYGB in T2DM remission in morbidly obese patients

Table 1 DiaRem scoring system

Factor	Score
Age (years)	
<40	0
40–49	1
50–59	2
≥60	3
HbA1C (%)	
<6.5	0
6.5–6.9	2
7–8.9	4
≥90	6
Other diabetic drugs	
No sulfonylureas or insulin-sensitizing agents other than metformin	0
Sulfonylureas and insulin-sensitizing agents other than metformin	3
Treatment with insulin	
No	0
Yes	10
Total score calculated by adding each of the four variables	0–22

Methods

Patient Selection and Study Design

We conducted a retrospective cohort study of patients with T2DM who underwent laparoscopic RYGB surgery in our tertiary care unit. We identified all morbidly obese patients who underwent laparoscopic RYGB between January 2018 and December 2018 from our database. All patients with BMI greater than or equal to 32.5 kg/m^2 were included in the study as per Obesity & Metabolic Surgery Society of India (OSSI) guidelines 2016 [9]. Patients without T2DM were excluded from the study. We defined type 2 diabetes according to American Diabetes Association (ADA) guidelines [10]: fasting blood glucose concentration $> 7.0 \text{ mmol/L}$ or HbA1C concentration of more than 6.5% (48 mmol/mol). The database included patient's age, gender, contact number, preoperative weight, preoperative BMI, T2DM status including HbA1C values, oral hypoglycaemic medications (metformin, sulfonylureas, insulin-sensitizing agents or other drugs) and usage of insulin. The details of patient's BMI, HbA1C and diabetic medications at a 1-year follow-up were recorded. Patients lost to follow-up were excluded from the study.

Definition of Diabetes Remission

Remission of diabetes is defined as per the ADA criteria [11]. Complete remission requires a fasting glucose $< 5.6 \text{ mmol/L}$ and an HbA1C below 6.0% for 1 year without the use of any diabetic medication. Partial remission is defined as fasting

Table 2 Characteristics of patients who underwent RYGB surgery with T2DM

Total patients included in the study (%)	55 (38.5)
Mean age in years	45.5
Gender	
Females (%)	34 (61.8)
Males (%)	21 (38.2)
Average preop BMI (SD) in kg/m^2	45.9 (8.2)
Average preop HbA1C (SD) in %	7.8 (1.7)
Diabetic medications	
Metformin (%)	45 (81.8)
Sulfonylureas and other ISA drugs (%)	10 (18.2)
Insulin (%)	10 (18.2)
DiaRem score	
0–2 (%)	13 (23.6)
3–7 (%)	23 (41.8)
8–12 (%)	9 (16.4)
13–17 (%)	6 (10.9)
18–22 (%)	4 (7.3)

SD standard deviation, ISA insulin-sensitizing agents

Table 3 Proportion of patients with DM remission according to their DiaRem score categories

DiaRem score category	Total, n	DM remission: CR + PR, n (%) at 1 year	CR (%)
All	55	40 (72.73)	33 (60)
0–2	13	12 (92.30)	12 (92.30)
3–7	23	20 (86.90)	15 (65.22)
8–12	9	5 (55.60)	3 (33.33)
13–17	6	2 (33.30)	2 (33.33)
18–22	4	1 (25)	1 (25)

CR complete remission, PR partial remission

glucose between 5.6 and 6.9 mmol/L and HbA1C between 6.0 and 6.5% for the duration of 1 year, in the absence of any diabetic medication. The records of patients were therefore analysed for the presence or absence of diabetes remission at least 12 months after RYGB surgery. We combined patients with “partial” and “complete” remission for the analysis in our study.

DiaRem Score Calculation

DiaRem scores were calculated for all eligible patients. Briefly, the DiaRem is a weighted score based on the sum of an age score, insulin dependence, diabetes medication use and HbA1C, ranging from 0 to 22 points (Table 1). Patients were stratified into groups by DiaRem score (0–2, 3–7, 8–12, 13–17 and 18–22). A low DiaRem score should predict high chances of diabetes remission, and high DiaRem score should predict low chances of diabetes remission [8].

Statistical Analysis

Preoperative BMI and HbA1C were compared with their post-operative values, respectively using paired *t*-test. *P* value less than 0.05 was considered significant. The predictive performance of the DiaRem was evaluated by areas under the

receiving operator characteristic (AUROC) curve. DiaRem cut-off score was also derived to predict DM remission with most optimal sensitivity and specificity. Analyses were conducted using the SPSS (Chicago, IL) for Windows Software, version 20.0.

Results

Patient Characteristics

One hundred and forty-three patients underwent RYGB surgery between January 2018 and December 2018, of which 61 patients (42.7%) had T2DM. Six patients lost to follow-up and were excluded. The final analysis included 55 patients (38.5%). Females were predominant (61.8%) compared to males (38.2%). The mean age of the population was 45.5 years. The mean BMI was 45.9 ± 8.2 kg/m². The mean HbA1C was $7.8 \pm 1.7\%$. The DiaRem score was calculated, and patients were stratified into five groups: 0–2, 13 patients; 3–7, 23 patients; 8–12, 9 patients; 13–17, 6 patients; and 18–22, 4 patients (Table 2).

1-Year DM Remission

The details of patients who followed for 1 year post-RYGB surgery were analysed retrospectively from the database. At 1 year, T2DM status was recorded which included HbA1C values and usage of diabetic medication. Five patients were

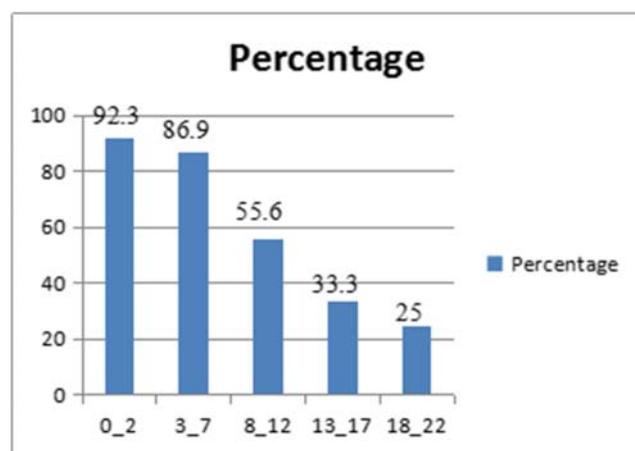


Fig. 1 DM remission in DiaRem score categories

Table 4 Paired *t*-test for pre- and post-op BMI

	Paired samples statistics				
	Mean	n	Std. Deviation	t	p Value
Preop BMI	45.93	55	8.16	21.352	<0.01
Post-op BMI	30.66	55	5.16		

The *p* value is less than 0.05, so the average pre-BMI is significantly different from average post-BMI

Table 5 Paired *t*-test for pre and post-op HbA1C

Paired samples statistics					
	Mean	n	Std. Deviation	t	p Value
Preop HbA1C	7.80	55	1.68	9.05	<0.001
Post-op HbA1C	6.02	55	0.64		

The *p* value is less than 0.05, so the average pre-HbA1C is significantly different from average post-HbA1C

contacted telephonically as they missed their 1-year follow-up visit. The DM remission rates of the patients categorized in the five DiaRem groups were noted as follows: 0–2, 92.30%; 3–7, 86.90%; 8–12, 55.60%; 13–17, 33.30%; and 18–22, 25% (Table 3 and Fig. 1). The average BMI at 1 year was $30.66 \pm 5.16 \text{ kg/m}^2$. The average HbA1C was 6.02 ± 0.64 . There was statistical significance between preoperative and post-operative BMI (Table 4) and HbA1C values (Table 5), respectively.

For predicting DM remission at a 1-year follow-up, a DiaRem cut-off score of 6.5 or less was found to have the most optimal sensitivity and specificity. The c-statistic (or area under the curve [AUC]) of 0.793 (95% CI 0.669–0.918;

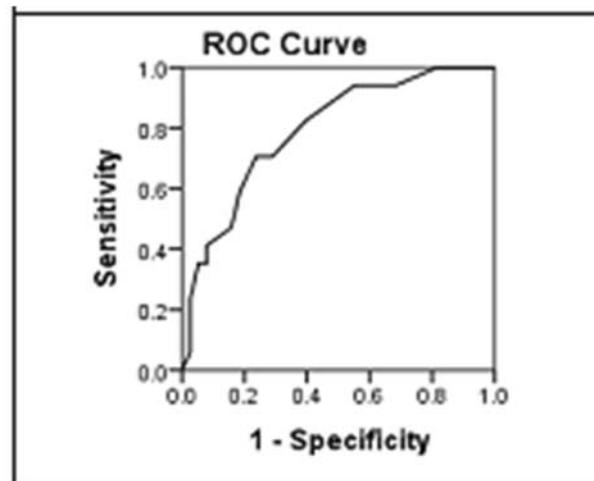
Fig. 2) indicates that the DiaRem score has a fair discriminative ability in predicting DM remission 1 year following RYGB surgery.

Discussion

Bariatric surgery is associated with significant rates of diabetes remission [12, 13]. It is important to identify the best responders to gain maximum benefit from bariatric surgery. A number of T2DM remission predictors have been developed over the past 10 years to better risk stratify obese patients with T2DM for bariatric surgery [14]. However, only two models, ABCD score [4] and the DiaRem score [8], have been externally validated in at least two independent cohorts. Both models were developed in patients who underwent RYGB; the ABCD model was initially verified in an Asian population, whereas the DiaRem score was verified in a US predominantly white cohort. A limited number of studies have directly compared the two scoring systems in terms of discrimination and calibration [15].

The DiaRem score is a simple scoring system which utilizes basic clinical parameters predicting the remission of diabetes following bariatric surgery. The original study by Still

Fig. 2 Area under the curve is 0.793 and the cut-off value is 6.50. The sensitivity at cut-off point is 0.706 and specificity is 0.763



Area Under the Curve

Test Result Variable: DiaRem score

Area	<i>P</i> -value	Asymptomatic 95% Confidence Interval	
		Lower Bound	Upper Bound
0.793	0.001	0.669	0.918

et al. in 2014 provided the first replication study using two additional cohorts to derive the DiaRem score and confirmed the predictive value of the DiaRem score [8]. In our cohort of 55 patients with T2DM who underwent RYGB, we found that the DiaRem score was predictive of DM remission at 1 year following RYGB surgery. In our study, 40 patients (72.73%) had DM remission (partial and complete) at 1 year post-RYGB. There were 33 patients (60%) who achieved complete remission. The proportion of patients with DM remission was more at lower scores compared to patients with higher scores. Only 25% of patients with scores of 18–22 achieved DM remission as compared to 92.30% of patients with scores between 0 and 2. Our analysis also showed that there was a significant decrease in BMI and HbA1C at a 1-year follow-up post-RYGB.

A study by Aminian et al. (2014) found a 49% complete diabetes remission rate among 136 patients within 1–2 years following RYGB surgery and found that lower DiaRem scores were associated with a greater likelihood of remission [16]. In their study, patients with a lower DiaRem score of 0–2 had high remission rates of 86% compared to 20% with a higher score group of 18–22. This was similar to our study. Other groups have conducted similar retrospective analyses and at a 1-year follow-up have found a higher proportion of patients with complete remission at lower DiaRem scores. However, these studies are limited by their small sample sizes [17, 18].

Few studies have proposed the optimal DiaRem cut-off score as a predictor of maximal benefit in terms of diabetes remission [19]. An optimal DiaRem score will help in patient selection and prioritization of patients most likely to achieve DM remission following surgical intervention. Therefore, determining a cut-off score most predictive of DM remission is of high clinical value. In our study, we found that a DiaRem score of 6.5 or less had the most optimal sensitivity and specificity, 70.6% and 76.3%, respectively, for DM remission post- RYGB.

In our study, remission rates of patients in the lower DiaRem score categories were similar to those reported by Still and colleagues, but there were differences in remission rates among those in higher categories. Similar results were obtained from other studies which showed better remission rates with poor DiaRem score [16, 18]. This has been the limitation of DiaRem score. There has been an attempt by different authors to improve the predictive accuracy of DiaRem especially in patients with poorer scores. Advanced DiaRem (Ad-DiaRem) score has been developed which includes 2 additional variables, i.e., duration of diabetes and number of glucose-lowering agents [20]. Similarly, DiaBetter scoring system which included duration of diabetes as additional variable has also shown an improved predictive value [21].

Another predictive score which has been validated externally is the ABCD score developed by Lee et al. [4]. ABCD score include four variables, i.e., age, BMI, C-peptide and

duration of diabetes. The score ranges from 0 to 10, and the higher the score, the greater the chances of DM remission. Lee et al. [22] compared the predictive power of both the scores (ABCD and DiaRem) for DM remission at 1 year post-RYGB. They concluded that ABCD score was better at differentiating patients with a poorer score (27.9% vs 9.1%, $p < 0.0001$). However, the ABCD score involves measurement of C-peptide which is costly and not easily available in routine practice [20], making it inconvenient to use especially in developing countries.

Our study has certain limitations that should be noted. The subject data is derived from a small cohort treated at the single institution. The study predicted short-term accuracy of the DiaRem score at 1 year and requires further follow-up of 5 years and 10 years to establish long-term validation of DiaRem to predict remission of T2DM following RYGB. Nonetheless, the DiaRem score has been validated in terms of long-term accuracy [17] as well as between different surgery types (LAGB, LSG and RYGB) [23].

The score acts as a guide for clinicians in patient selection and prioritization, and counselling to ensure maximal patient benefit from RYGB surgery. The short-term and long-term accuracy to predict T2DM remission has been validated in different studies. DiaRem score is based on basic clinical variables (age, HbA1C, medications and insulin) rather than on less conventional or non-standard biomarker like C-peptide used in ABCD score. In context of increasing burden on finances and limited resources especially in developing countries, the DiaRem score is easy to implement in clinical practice to guide both surgeons and patients.

Conclusion

The DiaRem score remains a useful preoperative tool to predict diabetes remission in patients with low scores (high chance for remission) but was more limited in its predictive power in those with a high score (least likely to have remission). Further work is required to develop a preoperative tool to identify patients based on preoperative health parameters for optimizing RYGB-induced diabetes remission in those people at highest risk.

Compliance with Ethical Standards

Conflict of Interest Authors declare that they have no conflict of interest.

Ethical Approval The study has been approved by the institutional ethical committee and review board.

Informed Consent For this type of study, formal consent was not required.

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