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ORIGINAL CONTRIBUTIONS

Predicting remission of diabetes post metabolic surgery: a comparison of ABCD, diarem, and DRS scores

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Abstract

Background Obesity is one of the major causes for development of T2DM. Metabolic surgery has been proved to be a successful and cost-effective treatment modality for managing the patients with obesity and T2DM. Many scoring systems and models have been described in literature to predict the outcome of T2DM after metabolic surgery. The aim of this study is to compare the efficacy of Diarem, DRS, and ABCD score in predicting the T2DM remission.

Methods A total number of 102 diabetic patients, who underwent LMGB/LOAGB, were selected for this study. A retrospective analysis of the three scoring systems when applied to these patients and their predictive abilities were analyzed.

Results At 1 year after surgery, 72 (70.59%) patients achieved remission of T2DM. Though the pairwise comparisons between AUC on ROC analysis of ABCD, Diarem, and DRS scores does not show statistically significant difference between them, Diarem score has the maximum relative area under ROC curves. By multivariate analysis, it was found that factors significantly associated with T2DM remission were duration of T2DM, C-peptide, and Pre-Op HbA1c.

Conclusions Among the three scoring systems, though DiaRem score has the best sensitivity and specificity and maximum AUC, no statistically significant difference was found in their diabetes remission predicting abilities. A shorter duration of T2DM, a lower HbA1C, and higher levels of C-peptide were significantly associated with a higher chance of T2DM remission.

Keywords T2DM (type 2 diabetes mellitus) · LMGB (laparoscopic mini gastric bypass) · LOAGB (laparoscopic one anastamosis gastric bypass) · AUC (area under curve) · ROC (receiver operating curve)

Introduction

According to International Diabetes Federation, 80% of people worldwide with T2DM are obese at the time of diagnosis. American Diabetes Association and the recent IFSO-APC statement have endorsed metabolic surgery as a treatment option for T2DM. Metabolic surgery has demonstrated good results in terms of glycemic control, improved HbA1C, and decrease in diabetic medication [1–3].

Since each metabolic surgery procedure is associated with some risks and complications, it is imperative to predict the patient who would respond to the surgery and will have diabetes remission. Several scoring systems like the one by Hayes et al. [4], Ramos Levi Am et al. [5], Lee et al. (ABCD score) [6], Still et al. (DiaRem score) [7], and Ugale et al. (DRS score) [8] for predicting T2DM outcome have been described in the literature. Recently, an Individualized Metabolic Surgery (IMS) Score has been proposed by Aminian et al. [9].

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The aim of this retrospective study is to compare ABCD score, DiaRem score, and DRS score for their ability and accuracy to predict remission of T2DM after metabolic surgery.

Material and Methods

Patient Selection

This retrospective study was conducted in the Department of Minimal Access and Metabolic Surgery, ILS Hospital, Kolkata, India. We identified patients who were enrolled in a metabolic surgery program for T2DM and obesity treatment from 2010 to 2015.The study was approved by the Hospital Ethics Committee.

The inclusion criteria were patients with T2DM, age between 18 and 65 years, BMI > 30 kg/m^2 and those who had completed 1-year follow-up. The exclusion criteria were the presence of end organ damage, previous gastrointestinal surgery, T1DM, and poor B cell function (i.e., diagnosis of type 1 diabetes, positive for antiGAD, islet cell auto-antibodies, fasting C-peptide levels < 1 ng/ml, unresponsive stimulus test).

For all the patients, a complete pre-operative work up and post-operative follow-up investigations were done. These included pre-operative HbA1C, fasting C-peptide, stimulated C-peptide (measurement of C-peptide 6 min after administration of 1 mg glucagon intravenously), and post-operative HbA1C.

In this study, partial (HbA1c < 6.5%) and complete remission (HbA1c < 6.0%) of T2DM for at least 1 year without anti-diabetes medications as described by Buse et al. [10], were combined together as remission and patients with HbA1c > 6.5 and those on anti-diabetic medication or insulin at 1-year follow-up were grouped as non-remission.

Interventions

All patients included in our study underwent laparoscopic mini gastric bypass (MGB)/laparoscopic one anastamosis gastric bypass (LOAGB). Informed consent was taken from all the patients. The laparoscopic MGB/OAGB was performed by Rutledge technique [11, 12].

Scoring Systems

The ABCD Score

Lee et al. [6] took the parameters of age, BMI, C-peptide level, and duration of diabetes for scoring (0–10). For age, 1 point was used. The each of remaining three variables had 4 categories and 0–3 points were assigned. Patients with higher ABCD scores were predicted to have a higher probability of T2DM remission after surgery.

DiaRem Score

Still et al. used a score of 0–22, having 4 variables [7]. A 4-point score, ranging from 0 to 3 was used for the factors of age and HbA1c level. For anti-diabetes drugs, 3-point score and for insulin treatment, 10-point score were used. The points for each variable were added. Patients with lower scores were predicted to have a higher probability of T2DM remission after surgery.

Diabetes Remission Score

Ugale et al. used this score for predicting the remission in patients with T2DM undergoing ileal interposition with sleeve gastrectomy (IISG) or ileal interposition with diverted sleeve gastrectomy (IIDSG) [8]. Seven variables, age, BMI, duration of T2DM, microvascular complications (retinopathy, nephropathy, etc.), macrovacular complications like CAD, pre-operative insulin use, and stimulated C-peptide, were included. Each of these seven variables was scored by a two-point scoring system. The score ranges from 7 to 12. Lower scores indicate a higher probability of achieving remission after surgery.

All the cut off values for each variable are shown in Table 1.

Statistical Analysis

Statistical analysis were performed using Statistica version 6 (Tulsa, Oklahoma: StatSoft Inc., 2001) and MedCalc version 11.6 (Mariakerke, Belgium: MedCalc Software 2011). Baseline comparisons were performed using chi-square tests and *T* tests. Continuous variables are expressed as the mean ± standard deviation. Differences in pertinent characteristics between patients who did and did not experience remission were established using the Mann-Whitney *U* test. A two-sided *p* value of 0.05 was considered statistically significant.

Results

Of the 115 T2DM patients who underwent metabolic surgical procedures between 2010 and 2015, 13 were lost to follow-up. The remaining 102 patients with at least 1 year of follow-up data were included in the study for further analysis.

The mean age was 45.63 ± 11.12 years (range 18–65 years), and mean BMI was 44.85 ± 9.24 kg/m^2 (range 30–76.0). The mean HbA1c level and disease duration were 8.26 ± 1.8% (range 5.1–13.2) and 5.3 ± 5.08 years (range 0.083–25), respectively. Five patients were on insulin exclusively, while

Table 1 ABCD, DIAREM, and DRS score

ABCD		DiaRem		DRS	
Factor	Score	Factor	Score	Factor	Score
Age (years)		Age (years)		Age (years)	
< 40	1	< 40	1	30–60	1
≥ 40	0	40–49	1	< 30 or > 60	2
		50–59	2		
		≥ 60	3		
				BMI (kg/m^2)	
				≥ 27	1
				≤ 27	2
BMI (kg/m^2)		HbA1c (%)		Duration of T2DM (years)	
< 27	0	< 6.5	0	< 10	1
27–34.9	1	6.5–6.9	2	≥ 10	2
35–41.9	2	7.0–8.9	4		
≥ 42	3	≥ 9.0	6		
				Microvascular complications	
				No	1
				Yes	2
C-peptide (ng/ml)		Other diabetic drugs		Macrovascular complications	
< 2	0	No sulfonylureas or insulin-sensitizing agents other than metformin	0	No	1
2–2.9	1			Yes	2
3–4.9	2				
≥ 5	3	Sulfonylureas and insulin-sensitizing agents other than metformin	3	Pre-operative insulin use	
				No	1
				Yes	2
Duration of DM (years)		Treatment with insulin		Stimulated C-peptide (ng/ml)	
> 8	0	No		≥ 4	1
4–8	1	Yes	0	< 4	2
1–3.9	2		10		
< 1	3				
Total score calculated by adding each of the four variables	0–10	Total score calculated by adding each of the four variables	0–22	Total score calculated by adding each of the seven variables	7–14

24 patients were on both oral medication and insulin. Seventy-three patients were only on oral anti-diabetic medication. The mean pre-operative C-peptide and stimulated C-peptide values were 3.80 ± 1.86 and 6.71 ± 2.65, respectively. There were no complications or surgical mortality in this series.

At 1 year after surgery, the mean percent excess body weight loss was 64.46 ± 19.39, mean weight decreased from 115.83 ± 25.64 kg to 82.21 ± 16.80 kg ($p < 0.05$), BMI decreased from 44.85 ± 9.24 to 31.65 ± 5.98 kg/m^2 ($p < 0.05$), and mean HbA1C decreased from 8.26 ± 1.8 to 5.96 ± 0.89 ($p < 0.05$).

Seventy-two (70.59%) out of 102 patients achieved remission of T2DM at the 1-year follow-up. Table 2 shows the comparison of characteristics between remission and non-remission group revealing significant differences in age, pre-op BMI, C-peptide, pre-op HbA1c, and duration of T2DM.

Table 3 shows the predictive abilities of the ABCD, DiaRem, and DRS score, respectively, for the probability of diabetes remission after gastric bypass surgery. Patients with lower DiaRem and DRS scores had a higher success rate of T2DM remission while patients with higher ABCD scores had a higher rate of T2DM remission.

Univariate analysis found that factors associated with T2DM remission were age, duration of T2DM, pre-op BMI, C-peptide, pre-op HbA1c, and pre-op use of insulin.

Multivariate analysis on T2DM remission factors revealed significant association of duration of T2DM, C-peptide, and pre-op HbA1c (Table 4). (Chances of T2DM remission

Table 2 Comparison of numerical variables between remission and non-remission groups

Characteristics	Remission (HbA1c < 6.5) ($N = 72$)	Non-remission (HbA1c > 6.5) ($N = 30$)	p value
Age (years)	43.67 ± 11.17	50.27 ± 9.70	0.006*
Pre-op BMI (kg/m^2)	46.39 ± 9.94	41.1 ± 5.95	0.008*
C-peptide (ng/ml)	4.10 ± 1.95	3.08 ± 1.40	0.011*
Stimulated C-peptide	7.02 ± 2.64	5.95 ± 2.56	0.063
Pre-op weight (kg)	118.31 ± 28.18	109.86 ± 17.09	0.1299
Pre-op HbA1c (%)	7.76 ± 1.55	9.48 ± 1.79	0.000*
Duration of DM	3.34 ± 2.99	10.01 ± 5.95	0.000*

*Statistically significant

decreased with the increase in duration of T2DM and pre-op HbA1c, and increased with the increase in C-peptide).

ROC Curve Analysis

On applying the receiver operating characteristic (ROC) analysis (Fig. 1), following results were seen:

- ABCD score of > 4 predicted remission with 90.3% sensitivity (95% CI 81.0–96.0%) and 56.7% specificity (95% CI 37.4–74.5%) with AUC (area under the ROC curve) 0.769.
- DRS score of ≤ 8 predicted remission with 88.9% sensitivity (95% CI 79.3–95.1%) and 60.0% specificity (95% CI 40.6–77.3%) with AUC 0.804.
- DiaRem score of ≤ 8 predicted remission with 91.7% sensitivity (95% CI 82.7–96.9%) and 66.7% specificity (95% CI 47.2–82.7%) with AUC 0.844.

Although the Diarem score had maximum AUC, on pairwise comparisons, there was no statistically significant difference between the AUC of the three scores (Table 4).

Discussion

There has been a steady rise in the prevalence of obesity and diabetes [13, 14]. In the Asian population, both of these are taking pandemic proportion more so in India. Several studies

Table 3 Predictive ability of scores

Score	N	Remission	Non-remission	Rate of remission (%)	Rate of remission (in literature) (%)
ABCD					
10–9	4	4	0	100	100
8–7	36	32	4	88.89	86.6
6–5	38	29	9	76.32	73.2
4–3	14	4	10	28.57	59.8
2–0	10	3	7	30	46.4
Total	102	72	30		
DiaRem					
0–2	16	16	0	100	88–99
3–7	47	40	7	85.12	64–88
8–12	13	10	3	76.90	23–49
13–17	13	3	10	23.08	11–33
18–22	13	3	10	23.08	2–16
Total	102	72	30		
DRS					
7–8	76	64	12	84.21	Mild
9–11	26	9	17	34.62	Moderate
12–14	–	–	–		Severe
Total	102	72	30		

Table 4 Multivariate analysis of T2DM remission factors and ROC analysis of scores

Variable	Co-efficient	*p* value	Adjusted odds ratio	95% CI of adjusted OR
Multivariate analysis of T2DM remission factors				
Age	−0.04261	0.1970	0.9583	0.8982 to 1.0224
BMI pre-op	0.01280	0.7950	1.0129	0.9197 to 1.1155
Duration of DM (year)	−0.3283	0.0004	0.7202	0.6005 to 0.8636
C-peptide	1.1727	0.0161	3.2306	1.2428 to 8.3979
Stimulated C-peptide	−0.4629	0.1005	0.6294	0.3623 to 1.0936
HbA1C pre-op	−0.6654	0.0022	0.5141	0.3356 to 0.7875
Pair wise comparison of ABCD, Diarem, and DRS scores				
	ABCD ~ DRS	ABCD ~ Diarem	DRS ~ Diarem	
Difference between areas	0.0345	0.0743	0.0398	
95% confidence interval	− 0.0958 to 0.165	− 0.0483 to 0.197	− 0.0461 to 0.126	
Significance level	$p = 0.6040$	$p = 0.2349$	$p = 0.3635$	

have shown efficacy of various metabolic surgical procedures in remission of T2DM [1, 15–18]. Different metabolic surgical procedures show different result in the rate of resolution of T2DM and co-morbidities. A perfect scoring system for predicting T2DM remission will assist the metabolic surgery team not only in proper selection of the patients but also in selecting the type of procedure to be performed. Our aim was to study the predictability of DRS, DiaRem, and ABCD scores in Indian population for remission of T2DM. We also analyzed individual factors associated with diabetes remission.

T2DM is a chronic progressive disease associated with progressive beta cell failure over the years [19]. Age, duration of T2DM, fasting and stimulated C-peptide levels, and pre-operative insulin use all reflect the beta cell reserve [4, 6]. Younger patients have a higher chance of T2DM remission and weight loss after metabolic surgery [20–23]. Older age groups have a poorer response [1, 16, 17, 24]. Similarly, the duration of DM is also inversely proportional to the chances of remission [15, 20, 24–27]. A higher C-peptide level, non-necessity of pre-operative use of insulin, and a low pre-operative HbA1c levels are positive predictors of T2DM remission [4, 20, 22, 25, 28, 29].

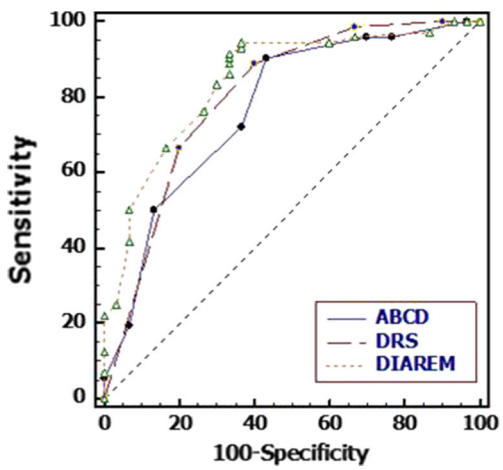

Fig. 1 ROC curve analysis of ABCD, Diarem, and DRS score

The role of BMI as a predictor of T2DM remission has been controversial. Robert et al. [30] in their study have shown that a BMI < 35 is a positive predictor for T2DM remission, whereas Dixon et al. showed an opposite of this result, BMI > 35 being a positive predictor [31]. Wang et al. found that baseline BMI played a role in T2DM remission only in Asian population [23], while some studies have shown no relation of baseline BMI with remission of T2DM [20, 32, 33].

Recently, Aminian et al. published the IMS score for calculating severity of T2DM. It included duration of T2DM, number of diabetes medications, insulin use, and glycemic control. In severe T2DM (IMS score > 95), there were low chances of remission [9].

In our study on univariate analysis, a younger age group, lesser duration of T2DM, lower levels of C-peptide and HbA1c, and patients not on insulin had a higher chance of T2DM remission. But on multivariate analysis of these factors, it was found that only the duration of diabetes, C-peptide, and HbA1C levels were significantly associated with T2DM remission.

In this study, it was observed that when DiaRem score was applied for predicting the remission of T2DM, remission rate in scores 18–22 and 8–12 were higher than what was published by Still et al. [7] (23.08 vs 2–16% and 76.90 vs 23–49%). Similar results of 25, 20, and 23% remission for 18–22 Diarem score were seen in studies by Lee et al. [34], Aminian et al. [35], and Tharakan et al. [36], respectively.

The DRS was divided into three grades as grade 1 (DRS 7–8), grade 2 (DRS 9–11), and grade 3 (DRS 12–14) [8]. In our study, 84.21% of patients scoring 7–8 had diabetes remission, whereas score 9–11 had 34.62% remission. There were no patients in subgroup 12–14.

Patients with greater ABCD had a better chance of success with T2DM remission (correlation ranging from 33% for

score 0 to 100% for score 10). A 1-point increase in the ABCD score translated to a 6.7% increase in the success rate [6]. This score has been externally validated by Lee et al. in two different studies [34, 37]. Although Praveen Raj et al. [20] found that a higher ABCD score was associated with higher likelihood of T2DM remission, this was statistically not significant. In our study, the lower ABCD score group (0–2, 3–4) showed a lower remission rate as compared to predicted remission rate (30 vs 33–47%, 28.57 vs 48–61%), respectively.

In our study, we have compared these three scores with the help of ROC curve. The AUC gave us the sensitivity and specificity of each scoring system for predicting the remission of T2DM. On applying ROC curve, it was noted that among these three scores, DiaRem score of < 8 had the maximum AUC of 0.844 and best sensitivity and specificity to predict the remission of T2DM, i.e., 91.7 and 66.7%. The AUC for ABCD score > 4 was 0.769 with sensitivity and specificity of 90.3 and 56.7%, respectively, while AUC for DRS was 0.804 with sensitivity and specificity of 88.9 and 60%, respectively. Though Diarem had maximum AUC, the pairwise comparison of these three scores did not show a statistically significant difference. This result could be because in all three algorithms, some of the factors represented the beta cell reserve directly or indirectly.

There were some difficulties in applying these scores. It was observed that while calculating DiaRem score, the use of insulin or sulphonylureas or insulin-sensitizing agent varied according to different practicing pattern in different geographic region as well as training of the physician. A similar observation was made by Thakaran et al. [36]. Also, DiaRem score did not include any duration of T2DM, one of the most important predictor of T2DM remission as proved by several studies. In DRS score, the percentage of remission in each of the three grades (mild, moderate, severe) were not mentioned which made it difficult to compare the outcome. The main limitation of this study was that it did not mention the differentiation between minor and major vascular complications. The inclusion of more variables in a scoring system would require further elaborate history taking and investigations. But ABCD score did not include HbA1c, a marker of glycemic control or chronicity of the disease and was a significant factor in our multivariate analysis. Also, HbA1c level is diagnostic criteria for T2DM and is usually done in all cases of T2DM, thus is easily accessible for scoring.

Limitation

This study had some limitations. The small size of study group from a single institute and a follow-up of only 1 year limited the scope of the study. In order to find out a perfect score for predicting the remission of T2DM, a multicentric prospective study with large population to cover various ethnic groups should be done. Also, a prolonged follow-up of the patients is required. As in other studies, Hb1AC 6.5 was taken as end point of diabetes remission in this study, but this overlooks the improvement in the T2DM status of the patient as suggested by the improvement in HbA1C level, reduction in antidiabetic medication, decrease in cardiovascular risk, and other T2DM-related complications [38].

Conclusion

Metabolic surgery is one of the most effective treatments for patients with obesity and T2DM. The chances of diabetes remission are inversely proportional to age of the patient, duration of T2DM, higher C-peptide level, and a higher BMI at the time of surgery. Patients with a higher HbA1C and those on insulin pre-operatively had a lower chance of diabetes remission. On multivariate analysis, only duration of T2DM, C-peptide, and HbA1c were significantly associated with T2DM remission. Among the three scoring systems, though DiaRem score has maximum AUC and the best sensitivity and specificity, no statistically significant difference was found in their diabetes remission-predicting abilities.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Statement of Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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