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Early outcome after laparoscopic sleeve gastrectomy of type two diabetes mellitus patients with extremely elevated glycated hemoglobin (HbA1c)



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ABSTRACT

Background: Due to high prevalence of type 2 diabetes mellitus (T2DM) and increasing popularity of bariatric and metabolic operations, Surgeons are faced with patients with relatively more severe T2DM disease. High level of glycated hemoglobin (HbA1c) is widely considered as a marker for uncontrolled T2DM. The aim of this study was to explore the correlation between high level of pre-operative HbA1c, peri-operative morbidity and post operative outcome after laparoscopic sleeve gastrectomy.

Methods: We conducted a retrospective study based on our medical center metabolic and bariatric registry. The inclusion criteria for selecting patients to the study group was HbA1c of 9 gram/dL and higher. A comparison control study was designed to include T2DM patients similar in all characteristics except for HbA1c of 7.5 gram/dL and less.

Results: We included 20 patients who underwent laparoscopic sleeve gastrectomy. Each group of patients included half of the patients. The mean pre operative HbA1c in the studied and the control group were 10.4 gram/dL and 7.1 gram/dL respectively ($p < 0.001$). There were no differences in peri-operative morbidity and length of stay at the hospital. Mean excess weight loss, fasting glucose levels and HbA1c levels were similar six months post surgery mean.

Conclusions: According to our study we have not found correlation between high HbA1c levels and increased peri-operative morbidity or insufficient excess weight loss among patients who underwent laparoscopic sleeve gastrectomy.

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1. Introduction

Bariatric and metabolic surgery provides excess weight loss and treatment of obesity related co-morbidities.^{1,2} Performing a bariatric operation on a patient who suffers from Type two Diabetes Mellitus (T2DM) is considered a highly effective procedure for controlling glucose blood levels and improving T2DM.³ In fact, currently this treatment resolves T2DM disease in up to 83% of the patients.⁴ However, this effect correlates with the degree of the disease. The remission rate of T2DM in patients who were diagnosed of T2DM 10 years or more prior to surgery is lower compare to other patients.⁵ While, several articles were published regarding the resolution of T2DM post-bariatric and metabolic surgery, the

peri-operative outcome of patients with T2DM has not been studied enough. The selection of which patient should not be operated due to advanced or severe uncontrolled T2DM is based on speculations and not by evidence based medicine. It is a common practice among many surgical teams to exclude patients from surgical treatment or at least to postpone further, scheduled operation due to high level of glycated hemoglobin (HbA1c). The assumption that patients with high HbA1c level are at greater risks of peri-operative morbidity and mortality is probably extrapolated from peri-operative outcome studies of non-bariatric procedures. However, these risks are related to the presence of T2DM and not necessarily to high levels of HbA1c which may play a role as a confounder. Facing the growing population of T2DM patients and the strong potential of bariatric and metabolic surgery in reversing the disease, these strategies and policies should be deduced from evidenced based studies. Therefore the aim of this study was to define whether the peri-operative risk and the short term outcome of T2DM patients allow performing sleeve gastrectomy in patients with very high HbA1c levels.

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2. Methods

The study was conducted as a retrospective study. We achieved the Institutional Review Board (IRB) approval for collecting and publishing data from the medical center's metabolic and bariatric registry. In this study, we included patients who underwent laparoscopic sleeve gastrectomy between April 2011 and September 2012. Our medical center metabolic and bariatric surgery service's policy is to encourage patients together with their primary care physicians to control glucose levels and improve T2DM prior to surgery. We recommend low carbohydrate and high protein preoperative diet with a calorie restriction of 800 kcal per day and three to five blood glucose measurements a day. Adjustments of oral anti diabetic medications or insulin injections are based on the patient's primary care physician or endocrinologist recommendations. Patients are re-evaluated at our clinic every two weeks. We keep with this process for 2 months. However, we do not exclude patient from operation if the patient has not lost weight unless we are convinced that efforts to lose weight and to control T2DM disease have not been taken. We also do not repeat blood test for Hb1Ac immediately prior to surgery. In this study we were seeking for data of T2DM patients with HbA1c levels of 9 g/dL and higher. This cutoff was quoted empirically due to: one, lack of definition of what extremely or very high levels are and two, due to lack of studies with such elevated mean HbA1c levels. In order to compare peri-operative morbidity, mortality and short term outcome, we matched a control group of T2DM patients who was similar to the studied group in all studied parameters except of HbA1c which was 7 g/dL and lower. The matched elements of both groups included: age, gender, body mass index (BMI) and years of T2DM prior to surgery. Percentage of excess weight loss was calculated relative to weight correlated with BMI of 25. Both groups were compared on the following variables: major peri-operative complications, Length of hospital stay post-surgery, re-admissions to the hospital in one month after the operation, percentage of excess weight loss and change in HbA1c six month post-surgery. We have not compared the qualitative factors of number and types of anti diabetic medications taken by patients due to our main aim of investigating the HbA1c quantitative variant. Due to small sample size we applied non parametric statistical analysis methods. Continue variables were presented as mean \pm standard deviation (SD) and the difference between them was deduced using the Mann–Whitney *U* test. Categorical data was compared using two tailed Fisher's exact test. Statistical significant difference was defined by a *p*-value of less than 0.01. The statistic power was calculated in order to assess statistically significant differences due to relatively small number of patients included in this study.

3. Results

Between April 2011 and September 2012 we performed 292 sleeve gastrectomy operations for treating obesity and its related co-morbidity. Thirty seven of these patients were diagnosed to suffer from T2DM disease. Out of this patients population we have found 10 patients who met the study inclusion criteria and visited the clinic 6 months following surgery with updated blood test results. We also matched a control group of patients which was designed according to the study protocol (Table 1). The mean \pm SD HbA1c levels of the studied and the control groups were 10.2 ± 1 and 7.1 ± 0.5 respectively. The mean \pm SD fasting glucose levels of the studied and the control groups were 218 ± 73 and 128 ± 23 respectively. Both differences were statistically significant ($p < 0.001$). The mean durations of T2DM disease in our study were 7.8 ± 6.6 and 4.4 ± 5.4 for the studied and the control groups (not statistically significant). The mean \pm SD time elapsed from first visit to the clinic to the operation was 2.4 ± 1.9 months. Comparing the peri-operative course has shown that mean hospital length of stay

was 4.7 and 5.2 days for the studied and for the control groups respectively (not statistically significant). In each group only one patient was re-admitted, it was due to fever and mild deep wound infection in the studied group and musculoskeletal pain not related to surgery in the control group. There were no other major complication including staple line leak.

Six months after the operation, mean excess weight loss in each group was 63% and 56% among the studied and the control groups respectively (not statistical significant). Also, the differences in parameters: BMI, fasting glucose and HbA1c level between the groups were not statistically significant. Not surprising, the mean percentage change of HbA1c in each group were 36% and 16% in the studied group and the control group respectively ($p < 0.001$).

The calculated statistical power of all parameters that was found to be statistically significant different was >0.76 (Tables 1 and 2).

4. Discussion

Treating patients with uncontrolled T2DM by metabolic operation is very effective. Laparoscopic sleeve gastrectomy is one of several procedures offered for treating morbid obesity and its related co-morbidities.⁶ The popularity that sleeve gastric procedure gains among surgeons is related to its simplicity and reproducibility. Its mechanism includes major caloric restriction, however, improvement of glucose control and T2DM before weight loss occurs together with human and animal experiments has raised several theories regarding mechanisms far beyond food restriction only.^{7–9} The total morbidity and major mortality rates of sleeve gastrectomy are fairly the same as for gastric bypass. The most fearful surgical type of morbidity is the gastric sleeve staple line leak which causes major patient inconvenience.¹⁰ According to studies the average rate of leak is less than 2.2%.¹¹ Although it usually resolves without re-operation, it heals very slowly and notoriously considered difficult to treat.

In this study we included T2DM patients with very high HbA1c levels. There is no consensus regarding not operating these patients. Searching the medical literature for articles describing studies on the correlation between HbA1c levels and peri-operative mortality and morbidity has shown controversy. Acott et al. published a retrospective study of 2960 T2DM who underwent major general surgery procedures.¹² Their study showed higher rates of peri-operative morbidity with no correlation to HbA1c levels. They concluded that peri-operative complications among T2DM patients may not be related to poor long term glucose control. Duckworth et al. have studied the effect of intense glucose control of T2DM patients with longstanding disease.¹³ The study included two groups of patients, one was intensively treated for T2DM and the second not. At the end of the study, the average HbA1c was 6.9 g%

Table 1
Preoperative patients' characteristics.

	High HbA1c group <i>n</i> = 10	Control group <i>n</i> = 10	Statistical power	<i>p</i>
Gender (m/f)	3/7	4/6		0.7
Age, years	50.3 ± 6.9	45.8 ± 12.7		0.59
BMI, kg/m ²	42.3 ± 3.9	41.3 ± 5.6		0.36
Years of T2DM	7.8 ± 6.6	4.4 ± 5.4		0.1
Fasting glucose, mg/dL	218 ± 73	128 ± 23	0.96	<0.001
HbA1c, g/dL	10.4 ± 1	7.1 ± 0.5	1	<0.001

Table 2
Post-operative patients' data.

Post-operative course	High HbA1c group <i>n</i> = 10	Control group <i>n</i> = 10	Statistical power	<i>p</i>
Post-operative complications	10%	0		0.7
Staple line leak	0	0		1
Post-operative length of stay, days	4.7 ± 0.9	5.2 ± 2.5		0.87
Post-operative re-admission	10%	10%		1
Six months post-operation				
BMI, kg/m ²	31.7 ± 4.1	32.3 ± 4.7		0.91
Excess weight loss%	61 ± 19	58 ± 17		0.73
Fasting glucose, mg/dL	113 ± 34	95 ± 13.5		0.138
HbA1c, g/dL	6.8 ± 0.8	6 ± 0.5	0.76	0.01
Decrease in HbA1c%	36 ± 9.3	16 ± 8	0.99	<0.001

and 8.4 g% in the intense treated group and control group (respectively). Also, they have not found any differences in rates of cardiovascular events, death and microvascular disease (except for microalbuminuria). On the other hand, as opposed to these studies, Adler et al., performed meta-analysis which showed a linear association between levels of HbA1c and the risk of lower extremity amputation in patients who suffers from T2DM.¹⁴

Interestingly, Rawlins et al. conducted a study of T2DM patients who underwent laparoscopic Roux en Y gastric bypass.¹⁵ They set a cutoff of 7 g/dL to select the patients to two groups. The mean HbA1c level of patients in the high level group was 9 g/dL. They concluded that patients with high HbA1c levels did not convey increased rate of morbidity or mortality. Comparing our study methodology to this study raises two major differences which we believe completes each other: One, we included patients who underwent sleeve gastrectomy as opposed to patients underwent gastric bypass. Second, we studied 10 patients in each group compare to 170 patients at their study. This size difference is a matter of an empiric decision related to cutoff setting. From our point of view setting the cutoff as high as possible and designing a control group of patients whose mean HbA1c level is significantly lower, potentiates our study conclusion that high HbA1c levels do not correlate with high morbidity and mortality in patients who underwent sleeve gastrectomy. Yip et al. conducted a study which compares post-gastric bypass weight loss between morbidly obese patients with and without T2DM.¹⁶ They concluded that the presence of T2DM has not influenced the excess weight loss. In our study we have not found any difference in weight loss related to the level of HbA1c. Numerous reports have discussed the influence of preoperative eating behavior on long term post-operative weight loss. However, in T2DM the most important predicting factor for short and long term post-operative T2DM improvement is the duration of the disease and not the level of preoperative glucose control. The mean duration of T2DM in our groups of patients was not statistically significant different but below ten years for both of them. Probably similarity in diseases' durations is a major determinant of physiologic equal potential for reversing T2DM disease. It is possible that if both groups would have included patients with longer durations of disease the results would have been different. We do believe that future studies should include large number of patients with long disease durations which will enable higher statistical power, multi variance analysis and logistic regression in order to study whether preoperative high HbA1c levels increases the post-operative morbidity and mortality in patients with long duration of T2DM disease.

Ethical approval

We have received our Institutional Review Board (IRB) to conduct retrospective studies using the bariatric patients' registry.

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None.

Author contribution

Ram Elazary operated patients, designed the study and wrote the article.

Mahmoud Abu Gazala designed the study and wrote the article.

Tair Ben Porat was in charge of the pre and post-operative dietician service, collected the data from the patients' registry, compared the variants and done the statistics.

Asaf Kedar collected the data from the patients' registry, compared the variants and done the statistics.

Yoav Mintz operated the patients and revised the article prior to submission.

Conflict of interest

All authors have no conflicts of interests to disclose.

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