The effect on glycemic status in type 2 diabetes mellitus after gastric cancer surgery

Lakshmi Rahakrishnan, T. V. Haridas*

Department of General Surgery, Government Medical College Thrissur, Thrissur, Kerala, India

Received: 13 October 2020
Revised: 05 December 2020
Accepted: 08 December 2020

*Correspondence:
Dr. T. V. Haridas,
E-mail: tvharidas2020@gmail.com

ABSTRACT

Background: Gastric cancer is a leading cause of cancer death worldwide. With progress in the field of gastric cancer treatment, as indicated by the improved survival rate, postoperative quality of life as well as the appropriate surgical treatment for a cure has become very important. Recently, metabolic surgery has become an appealing treatment option for patients with type 2 DM. Although the purpose of metabolic surgery and gastric cancer surgery is completely different, they are related clinically and technically. Thus organized evaluation of the impact of gastric cancer surgery on diabetes is necessary.

Methods: 30 patients with gastric cancer and type 2 DM who underwent curative gastrectomy were selected. Patients were followed up till 12 months, the study population grouped depending upon the glycemic status and results compared using chi square test.

Results: Three out of 30 patients had complete remission of diabetes at 12 months, 17 patients improved and 10 patients remained stationary. Short duration (<5 years) had a median reduction in insulin by 8.9 units versus 2.5 units in long duration (>10 years) diabetes. Maximum reduction (>10 U/day) and remission occurred in those who underwent total gastrectomy. The results were compared using chi square test and the p value was 0.048428 (<0.05) proving significant.

Conclusions: The glycemic status was found to improve following gastric cancer surgery which was found to be related to the extent of gastrectomy and the diabetes duration and was found to be statistically significant.

Keywords: Gastrectomy, Gastric cancer, Type 2 diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is associated with obesity and metabolic derangements, leading to increased morbidity and economic burden. Although population-based efforts through lifestyle interventions are essential to prevent and deal with the parallel epidemics of obesity and T2DM only a few patients who have already developed T2DM and obesity are able to comply and accomplish long term weight loss and glycemic control.1

Given its role in metabolic regulation, the gastrointestinal tract constitutes a biologically and clinically meaningful target to treat Type 2 DM, especially in light of accumulating experimental and clinical evidence that surgery with gastrointestinal manipulations might result in type 2 DM remission.2

Surgical operations with intestinal diversion and mainly duodenal-jejunal exclusion, has consistently shown beneficial effects on glucose homeostasis by reducing insulin resistance and increasing insulin secretion.3 Mechanistic evidence further suggests that the bypass or exclusion of the duodenum and jejunum (proximal gut) may exert direct beneficial effects on glycemic control beyond those mediated by weight loss.4 The widely used
term “metabolic surgery” applies to those types of weight loss surgery modalities involving an anatomical bypass of the upper gastrointestinal tract and functional remodelling of the intestine, which has been shown to give the most important benefits with regard to glucose homeostasis.³

In a systematic reviews and meta-analyses of randomized clinical trials (RCT) comparing surgical to non-surgical treatment of morbid obesity, bariatric surgery was associated with greater weight loss, higher remission rate of T2DM and metabolic syndrome, better lipid profile, greater improvement in quality of life, and substantial reductions in medication requirements.⁵ Furthermore, a growing number of recent RCTs in patients with Type 2 DM, sliding mainly individuals with BMI 35 Kg/m², have consistently so many demonstrated superior efficacy of bariatric surgery in reducing weight and lowering glycemia, compared to a variety of medical and lifestyle interventions.⁶⁻¹³

**Objective**

To evaluate the effect of gastrectomy on diabetes control in patients with type 2 diabetes mellitus and early gastric cancer.

**METHODS**

The study was conducted in the General Surgery Department of Government Medical College, Thrissur. This cross sectional study involves patients who are diabetic with a diagnosis of early gastric cancer, who eventually required surgery on an elective basis. Details of consecutive patients subjected to elective gastrectomy (subtotal/total) were collected, study was limited to patients with early gastric cancer. Those who were diagnosed to have advanced malignancy and those who underwent neoadjuvant chemotherapy were excluded from the study.

**Sample size calculation:** Confidence interval: 95% (Z), Precision of study: 0.1 (d)

Prevalence (P) 81.8% (Wang et al).

P: proportion of diabetic patients who undergo gastric cancer surgery who achieve improvement in glycemic status

D: 20% maximum allowable error/precision

Formula: \( Z^2P(1-P)/d^2 \)

Sample size: 22

Study period: 1 year (September 2016-September 2017).

All participants were provided written informed consent. A total of 30 patients were included in the study. Data were obtained by the investigator from patient interviews with the help of a verified proforma, together with reviews of primary care and hospital records. Data obtained from patient interviews included name, age, sex, IP no, duration of diabetes, medications taken, glycaemic control, diagnosis of gastric malignancy, OGD report, biopsy details and surgery planned. Patients were followed up in the intra operative as well as the postoperative time period for obtaining the precise diagnosis.

Histopathology examination specimens were sent to central lab of Government Medical College, Thrissur for detailed evaluation for all patients. HPR records of the hospital were reviewed at a later date to confirm the diagnosis. Post operatively at 3, 6 and 12 months and the glycaemic status is assessed by HBA1C and insulin requirement along with FBS/PPBS. Data are presented as numbers or percentages and analysed with the help of a statistician. Independent variables were assessed by Chi-square test. This study was approved by Institutional research committee and ethical committee.

**RESULTS**

A total number of 30 patients with early gastric cancer and type 2 DM were analysed who underwent curative gastrectomy. A total of 24 male patients and 6 female patients were candidates in the study with a mean age of 64.8 years.

**Table 1:** Age distribution of patients.

| Age distribution (in years) | No. of patients |
|----------------------------|----------------|
| <50                        | 2              |
| 51-60                      | 8              |
| 61-70                      | 13             |
| 70-80                      | 6              |
| >80                        | 1              |

The average duration of diabetes was 9.3 years with a range of 3-25 years out of which most of patients had a diabetic duration of ≤5 years or 10-20 years.

**Table 2:** Duration of diabetes.

| Duration of diabetes | No. of patients |
|----------------------|----------------|
| ≤5 years             | 11             |
| 5-10 years           | 6              |
| 10-20 years          | 11             |
| >20 years            | 2              |

Patients had preoperative conversion of OHA to insulin to attain euglycemic status; hence improvement in glycemic status was assessed by decrease in insulin requirement to maintain normal blood sugar levels. The
mean insulin requirement preoperatively was 10.4 units/day.

All surgeries were done by open approach; via a laparotomy. Out of 30 patients, 22 patients underwent subtotal gastrectomy followed by Billroth II anastomosis and 8 patients underwent total gastrectomy and Roux-en-Y esophagojejunostomy. All the patients underwent curative resection RO, with lymph node dissection. Specimen was sent for HPE for confirmation of diagnosis and pathological staging.

In the 30 patients studied, preoperative mean insulin requirement was 10.4 units in 24 hours; with a range of 6 to 48 units/day; after curative gastrectomy, a steady drop in insulin requirement was noticed and at the end of 12 months it was 8.15 Units/24 hours. Most patients had a decrease in insulin requirement of about less than 10 units (46.6%) while no change was seen in 11 patients. 5 patients had a reduction of insulin requirement by 10 or more units than the preoperative requirement and all of them had undergone total gastrectomy with Roux-en-Y esophagojejunostomy.

Figure 1: Mean insulin requirement trend.

The mean insulin reduction between the preoperative period and at 12 months was found to be 8.9 in patients with diabetic history less than or equal to 5 whereas the same with more than 10 years diabetes duration was only 2.5 Hence the extent of insulin reduction was found to be inversely related to the diabetes duration; i.e. shorter the duration of diabetes greater was the reduction in insulin requirement.

At the end of 12 months, the study population of 30 patients was divided into 3 groups based on the current diabetic status. These were as follows:

**Remission:** 3 out of 30 patients (10%) had complete remission of diabetes; i.e; attained euglycemia without medications.

**Improved:** 17 out of 30 patients (56.66%) had improvement in diabetic status as indicated by reduction in insulin requirement to achieve euglycemia.

**Stationary:** 10 patients (33.3%) had no significant improvement in glycemic status as compared to the preoperative period.

Among the total gastrectomy group, 3 patients (37.5%) went into remission and remaining 5 (62.5%) patients improved in their diabetic status. Whereas in the subtotal gastrectomy group, no patients went into remission. 11 (50%) patients remained stationary and 11 (50%) patients improved. Thus improvement in diabetic status was more following total gastrectomy when compared to subtotal gastrectomy.

**DISCUSSION**

Among the 30 patients who underwent elective radical gastrectomy (subtotal total gastrectomy) for early gastric cancer, the highest number of members in the 61-70 years age group. Mean age of the study group was 64.866 years with a SD of 8.327 years. According to the American Cancer Society estimates for stomach cancer in the United States, the average age of people when they are diagnosed is 68. About 6 out of 10 people diagnosed with gastric cancer each year are 65 years or older. In India, gastric cancer incidence is found to be highest in Mizoram where hospital based data show the male female ratio was 2.3:1; the median age for males was 58 years and that for females was 57 years. Among the 30 patients studies, 6 were female and 24 male, which is a far greater sex ratio than global and Indian average.

Mean BMI at initial observation was 30.32373 kg/m² (SD 4.17 kg/m²). Mean BMI after 3, 6 and 12 months were 2917388±3.90 kg/m², 28.08146±3.94 kg/m², 26.801±3.15 kg/m² respectively. Many studies have shown higher risk for gastric cancer in obese patients with high BMI. In our study a steady decrease in BMI was noted post operatively although the preoperative BMI was on the higher side. A study by Luu et al, division of Surgical Oncology, California, of 168 patients showed a steady decrease in BMI postoperatively irrespective of type of gastrectomy, subtotal/total. The improvement in glycemic status has been assessed by the decrease in insulin requirement postoperatively so as to maintain normal blood sugar levels measured by fasting and post prandial blood glucose estimations and HbA1c.

A decreasing trend in the mean insulin requirement was noted with a mean Requirement of 10.4 units/day preoperatively to requirement of 8.15 unit/day postoperatively at the end of 12 months. The reduction in insulin requirement was found to be inversely related to diabetes duration; short duration (<5 years) a mean reduction in insulin by 8 units compared to 2.5 units in long duration (>10 years) of diabetes. The maximum insulin reduction was seen in patients who underwent total gastrectomy as compared to subtotal gastrectomy.
It is possible that the islet function is less impaired in patients with a shorter duration of type 2 diabetes than in patients with a longer duration of diabetes.

A decreasing trend of mean HbAlc at the end of 12 months was noted in our study group and was slightly more in the total gastrectomy group than subtotal gastrectomy.

Among the 30 patients studied, 3 patients had complete remission at 12 months so as to attain normoglycemia without medications, while 10 patients had no significant change in insulin requirement hence fell into the stationary group. Remaining 17 patients had slight to marked decrease in insulin requirements, much greater towards the end of 12 months; hence improved glycemic status.

In recent studies which evaluated diabetes remission after gastric cancer surgery, diabetes remitted in 15.1-19.7% of the patients with gastric cancer. In our study, the rate of diabetic remission rate was 10% and was seen in patients underwent total gastrectomy.

Limitations of the study were patients who were not willing for regular followup or testing postoperatively; any error or incomplete data entry; study does not include patients with type 1 DM; patients who leave against medical advice.

CONCLUSION

Development of diagnostic tools and use of mass screening programs has recently contributed to increased early detection and prolonged survival of gastric cancer patients. Comorbid disease has emerged as the main cause of mortality in gastric cancer patients, rather than malignancy itself, especially at earlier stages, with type II diabetes mellitus (DM) being the most common comorbidity.

By this study, one can conclude that there is a marked improvement in the glycemic status and thereby decrease in insulin requirement in a substantial proportion of the study population which points towards the effectiveness of onco-metabolic surgery. Also, we noticed better glycemic control is obtained in subjects who underwent total gastrectomy and patients with a shorter duration of diabetes.

Recommendations

Although diet, exercise, and pharmacotherapy are the primary therapeutic options for treating this progressive disease, surgery may hence be also considered effective treatment modality for managing Type 2 DM. There is growing need of further research work in the field of onco-metabolic surgery and focus needs to be given to both aspects of the disease in order to attain a better quality of life.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Catol AF, Pärvu A, Murjan A, Busetto T. Metabolic mechanisms in obesity and type 2 diabetes: insights from bariatric metabolic surgery, Obes Facts. 2015;83:50-63.
2. Cefalu WT, Rubino F, Cummings DE. Metabolic surgery for type 2 diabetes: changing the landscape of diabetes care. Diabetes Care. 2016;39(6):857-60.
3. Rubino F, Schauer PR, Kaplan M, Cummings DE. Metabolic surgery to treat type 2 diabetes: clinical outcomes and mechanisms of action Anna Rev Med. 2010;61:393-411.
4. Rubino F, Marescaux J. Effect of duodenal-jejunal exclusion in a non-obese animal model of type 2 diabetes: a new perspective for an old disease. Ann Surg. 2004;239(1):1.
5. Gloy VL, Briel M, Bhi DL Kashyap SR. Schauer PR. Mingrone G, et al. Bariatric surgery versus surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347:f5934.
6. Mingrone G, Panunzi S, De Gaetano A, Guidon C, Iaconelli A, Leccesi L, et al. Bariame surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med. 2012;366:1577-83.
7. Schauer PR, Kashyap SR, Wolski K, Brethauer SA, Kirwan JP, Pothier CE, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med. 2012;366(17):1567-76.
8. Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Nanni G, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet. 2015;386(9997):964-73.
9. Cummings DE Artertum DE, Westbrook EO, Kurma IN, Stewart SD, Chan CP, et al. Gastric bypass surgery vs intensive lifestyle and medical intervention for type 2 diabetes: the CROSSROADS randomised controlled trial Diabetologia. 2016;59:945-55.
10. Halperin F, Ding SA, Simonson DC, Panosian J, Goebel-Fabbri A, Wewalka M, et al. Roux-en-Y gastric bypass surgery or lifestyle with intensive medical management in patients with type 2 diabetes: feasibility and 1-year results of a randomized clinical trial. JAMA Surg. 2014;149(7):716-26.
11. Ikramuddin S, Korner J, Lee WJ, Connelt JE, Inabnet WB, Billington CJ, et al. Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study
randomized clinical trial. JAMA. 2013;309(21):2240-9.

12. Courcoulas AP, Goodpaster BH, Eagleton JK, Belle SH, Kalarchian MA, Lang W, et al. Surgical vs medical treatments for type 2 diabetes mellitus: a randomized clinical trial. JAMA Surg. 2014;149:707-15.

13. Courcoulas AP, Belle SH, Neiberg RH, Pierson SK, Eagleton JK Kalarchian MA, et al. Three-year outcomes of bariatric surgery vs lifestyle intervention for type 2 diabetes mellitus treatment: a randomized clinical trial. JAMA Surg. 2015;150:931-40.

14. Phukan RK, Zomawia E, Hazarika NC, Baruah D, Mahanta J. High prevalence of stomach cancer among people of Mizoram, India. Curr Sci. 2004;285-6.

15. Luu C, Arrington AK, Falor A, Kim J, Lee B, Nelson R, et al. Impact of gastric cancer resection on body mass index. Am Surg. 2014;80(10):1022-5.

Cite this article as: Rahakrishnan L, Haridas TV. The effect on glycemic status in type 2 diabetes mellitus after gastric cancer surgery. Int Surg J 2021;8:191-5.