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Original Research Article

Post-operative morbidity and mortality following D2 gastrectomy in a state funded tertiary care centre in South India

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ABSTRACT

Background: Radical gastrectomy with D2 lymphadenectomy is a surgery with significant post-operative morbidity. Pre-operative malnutrition portends a poor post-operative outcome following any gastrointestinal surgery in general. This study aims at finding out whether it is feasible to perform D2 lymphadenectomy in patients presenting with significant malnutrition.
Methods: In this single centre study, we retrospectively analysed the post-operative morbidity and mortality data of 46 patients who underwent D2 gastrectomy for operable gastric cancer between October 2016 to April 2019. Almost all the patients who were analysed fulfilled at least one criterion for malnutrition.
Results: The morbidity rate was 39.1% and the mortality rate was 6.5% which were a little high when compared to results from other Indian centres but not prohibitive, considering the nutritional status of these patients. Almost 50% of these patients were able to complete adjuvant chemotherapy.
Conclusions: D2 gastrectomy can be performed in patients with poor pre-operative nutritional status. If perioperative nutritional requirements are taken care of promptly, the post-operative outcomes can be better.

Keywords: D2 gastrectomy, Malnourished, Post-operative morbidity

INTRODUCTION

The incidence of gastric cancer is on the decline in India, similar to the rest of the world, but with wide geographical variations. The incidence rate of stomach cancer in males varies widely among registries, highest being 11.1 per 100,000 in Chennai compared to 1.6 per 100,000 in Bhopal.[1] Surgical resection offers the only chance of cure in localized Gastric cancer.[2,3] The extent of surgery, the lymphadenectomy part in particular, has been a subject of great controversy over the past two decades.[4,5] Radical gastrectomy with D2 lymphadenectomy is now considered as the standard of surgical care in both eastern and western centers.[6] This paradigm shift has brought in newer difficulties in the management of patients who belong to the low socioeconomic group. Combination of adverse features like delayed presentation, significant weight loss, advanced nature of disease increases the risks of surgery several fold. A vast majority of the patients who are treated in the teaching hospital where this study was conducted belong to the low socioeconomic group and present in advanced stages. Protein calorie malnutrition is the rule in these patients.[7,8,9] Even though the mortality rates following a D2 gastrectomy is not significantly different from D1 gastrectomy, the morbidity rates are shown to be as high as 50% in some studies and even

higher if the resection involves removal of multiple organs.[10,11,12,13] Malnutrition, in general has been shown to have a major morbidity rate of 30-35% following gastrointestinal surgery.[14,15] Whether it is feasible to perform such an extensive surgery in patients who are invariably malnourished, belong to low socioeconomic class, present late with advanced disease remains to be explored. Additionally, whether these patients can withstand and complete the adjuvant chemotherapy regimen is also a problem to be addressed.

METHODS

This retrospective study included 46 patients treated in the Institute of Surgical Gastroenterology, Madras Medical college, Chennai, India who presented with operable gastric cancer in the period between October 2016 to April 2019. Data was retrieved from the previous medical records. All patients were evaluated with complete blood count, liver function tests and cardiopulmonary evaluation.

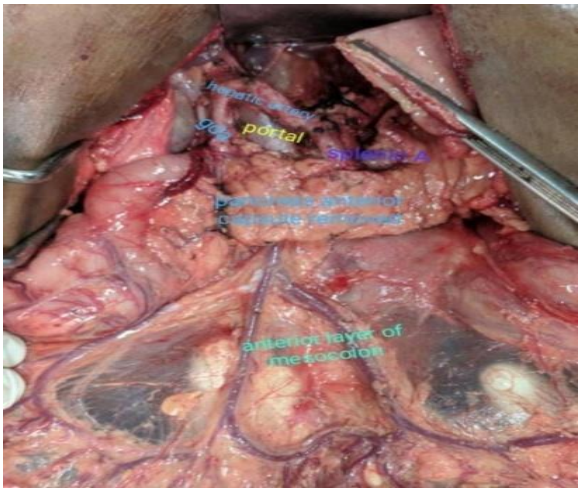

Figure 1: Bursectomy.

Esophagogastroduodenoscopy and biopsy, CT scan of the abdomen and pelvis were done in all patients to diagnose and stage the disease. Patients with type3 Sieverts Junctional cancer who underwent extended gastrectomy involving resection of distal esophagus with D2 Lymphadenectomy were not included. Patients with liver metastasis, peritoneal seedlings, malignant ascites or extensive adjacent organ involvement that is deemed unresectable on CT were excluded from the study. Diagnostic laparoscopy was performed in select patients as a part of staging. Cancer staging was based on the eighth edition of the Union for International Cancer Control (UICC) TNM classification system.[16] None of the patients in this study received neoadjuvant therapy. All patients who underwent D2 gastrectomy irrespective of the final histopathological diagnosis were included in the study. The extent of gastric resection (distal or total) was dictated by the ability to give a proximal resection margin of 5 cm. In addition the preoperative nutritional status of the patients was also evaluated with serum Albumin level, body mass index and amount of weight loss.[17,18]

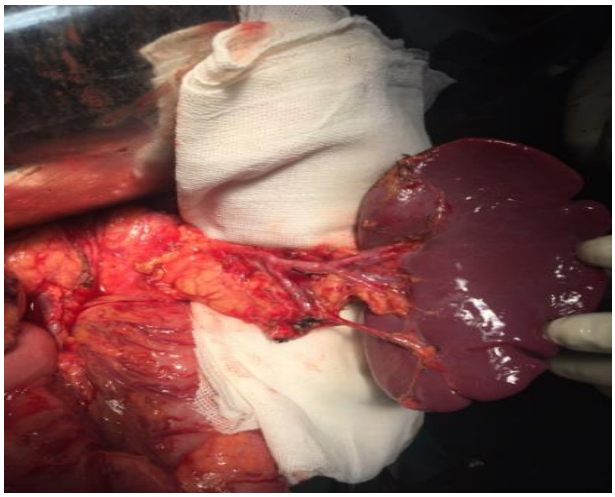

Figure 2: Level 10 nodal dissection.

By an upper midline incision abdominal exploration was done to detect metastatic disease in the liver, pouch of Douglas or other organs that were not detected by preoperative CT examination. Intraoperatively, the location of the tumour and the presence of serosal disease and adjacent organ involvement was assessed. The omentum was detached from the colon and dissection was continued onto the transverse mesocolon, taking the anterior layer of the mesocolon with the omentum and taking care not to damage the colonic vasculature. The division of right gastroepiploic, right gastric, left gastric vessels, followed by duodenal, and gastric/esophageal transection was done sequentially. D2 lymphadenectomy included removal of stations 1 to 12a group of lymph nodes. For a total gastrectomy: D0 lymphadenectomy includes anything less than D1; D1 includes dissection of level 1 to 7; D1+ includes D1 lymph nodal dissection and stations 8a, 9 and 11p; D2 incorporates D1 lymph nodal dissection and stations 8a, 9, 10, 11p, 11d and 12a. For tumors involving the distal esophagus, D1+ includes dissection of 110 while D2 includes dissection of 19, 20 and 111. For a distal gastrectomy - D0 lymphadenectomy includes anything less than D1; D1 includes dissection of level 1, 3, 4sb, 4d, 5, 6 and 7; D1 + includes D1 lymph nodal dissection and stations 8a and 9; D2 incorporates D1 lymph nodal dissection and stations 8a, 9, 11p, and 12a.[19] Reconstruction following subtotal gastrectomy was performed by loop gastrojejunostomy and for total gastrectomy, reconstruction was carried out by Roux-en-Y esophagojejunostomy. Postoperative surgical complications were graded according to the Clavien–Dindo classification.[20] The objective variables were morbidity C-D grade II or higher, and patients with complications of less than grade II were considered no-complication. When two or more complications occurred in one patient, the higher grade was adopted. Major complications were defined as morbidity C-D grade III or higher. The operative time was measured from the time

of trocar insertion to the time of abdominal closure. The amount of intraoperative blood loss was determined according to the volumes and weights of suction pumps and surgical gauze during gastrectomy. Patients who were at a disease stage >T2, N0 were administered adjuvant therapy. The adjuvant therapy included 5-fluorouracil and cisplatin. Data analysis was done by simple statistical analysis.

Table 1: Anatomical definitions of lymph node stations.[19]

LNs	Definitions
1	Right paracardial LNs, including those along the first branch of the ascending limb of the left gastric artery
2	Left paracardial LNs including those along the esophagocardiac branch of the left subphrenic artery
3a	Lesser curvature LNs along the branches of the left gastric artery
3b	Lesser curvature LNs along the 2nd branch and distal part of the right gastric artery
4sa	Left greater curvature LNs along the short gastric arteries (perigastric area)
4sb	Left greater curvature LNs along the left gastroepiploic artery (perigastric area)
4d	Rt. greater curvature LNs along the 2nd branch and distal part of the right gastroepiploic artery
5	Suprapyloric LNs along the 1st branch and proximal part of the right gastric artery
6	Infrapyloric LNs along the first branch and proximal part of the right gastroepiploic artery down to the confluence of the right gastroepiploic vein and the anterior superior pancreatoduodenal vein
7	LNs along the trunk of left gastric artery between its root and the origin of its ascending branch
8a	Anterosuperior LNs along the common hepatic artery
8p	Posterior LNs along the common hepatic artery
9	Coeliac artery
10	Splenic hilar LNs including those adjacent to the splenic artery distal to the pancreatic tail, and those on the roots of the short gastric arteries and those along the left gastroepiploic artery proximal to its 1st gastric branch
11p	Proximal splenic artery LNs from its origin to halfway between its origin and the pancreatic tail end
11d	Distal splenic artery LNs from halfway between its origin and the pancreatic tail end to the end of the pancreatic tail
12a	Hepatoduodenal ligament LNs along the proper hepatic artery, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
12b	Hepatoduodenal ligament LNs along the bile duct, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
12p	Hepatoduodenal ligament LNs along the portal vein in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
13	LNs on the posterior surface of the pancreatic head cranial to the duodenal papilla
14v	LNs along the superior mesenteric vein
15	LNs along the middle colic vessels
16a1	Paraaortic LNs in the diaphragmatic aortic hiatus
16a2	Paraaortic LNs between the upper margin of the origin of the celiac artery and the lower border of the left renal vein
16b1	Paraaortic LNs between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery
16b2	Paraaortic LNs between the upper border of the origin of the inferior mesenteric artery and the aortic bifurcation
17	LNs on the anterior surface of the pancreatic head beneath the pancreatic sheath
18	LNs along the inferior border of the pancreatic body
19	Infradiaphragmatic LNs predominantly along the subphrenic artery
20	Paraesophageal LNs in the diaphragmatic esophageal hiatus
110	Paraesophageal LNs in the lower thorax
111	Supradiaphragmatic LNs separate from the esophagus
112	Posterior mediastinal LNs separate from the esophagus and the esophageal hiatus

LNs: Lymph nodes.

RESULTS

The majority of the studied patients were males (38 males and 8 females). The male to female ratio was 4.8:1. The ages ranged from 28 to 77 years and the mean age was 58.3 years. The tumor was located in the pyloric antrum in 29 patients (63%), gastric body in 17 (37%) patients. Patients with more than 10% loss of body weight in the last 6 months or BMI less than 18.5 or serum albumin level less than 3.0 g/dl were considered as malnourished. Except two patients all others fulfilled at least one criteria for malnourishment. Pulmonary comorbidities, most of

them associated with smoking, was found to be the most common comorbidity.

Intra operative findings were as follows: in 16 patients the tumor did not reach the serosa, while the serosa was apparently involved without invading nearby organs in 13 patients. Invasion of the transverse colon was encountered in one patient. The mean number of lymph nodes dissected and examined pathologically was 17.8 (range from 10–28) LNs. Metastatic deposits in lymph nodes were detected in 41 cases; According to TNM staging system, 13 patients had N0 stage, 20 patients had N1 stage and 7 patients had N2 stage and 11 patients had N3 nodal stage.

In one case left lateral segmentectomy was done en bloc with gastrectomy. Right colectomy and splenectomy was also done enbloc with gastrectomy in one case were the tumor was found to invade the serosa of the transverse colon. The mean operative time was 273 min. In one patient significant blood loss needed massive transfusion. No intraoperative complications were encountered in other patients. The mean blood loss was 233 ml.

Table 2: Demographic data.

Characteristics	D2 gastrectomy (n=46)
Age (years)	54.26 (28–77)
Sex	
Male	38 (82.6%)
Female BMI (kg/m^2)	8 (17.4%)
<18.5	25 (54.3%)
≥18.5	21 (45.7%)
Weight loss	
<10%	3 (7%)
≥10%	43 (93%)
ASA scores	
1	2
2	13
3	30
4	1
No. of comorbidities	
0	33
1	11
2	1
≥3	1
Comorbidity	
Hypertension	2
Diabetes	11
Pulmonary	1
IHD	0
NIL	33
Others	0
Tumor location	
Antropyloric	29 (63 %)
Body	17 (37%)
HB (g/l)	9.2
ALB	
<3 g/dl	36 (78%)
≥3 g/dl	10 (22%)
P stage	
IA	1
IB	3
IIA	7
IIB	10
IIIA	13
IIIB	12
IIIC	0

Table 3: Complications.

Variables	D2 gastrectomy (n=46)
Overall complications	18 (39.1%)
Major complications	10 (22.2%)
Surgical complications	19.6%
Abdominal infection	-
Anastomotic leakage	1
Intra-abdominal bleeding	0
Intestinal obstruction	1
Gastroparesis	2
Incision-related complications	5
Chylous leak	-
System complications	19.5%
Pneumonia	4
Pleural effusion	1
Acute kidney injury	0
Urinary tract infection	4
Mortality	3 (6.5%)

Table 4: Surgical outcomes.

Variables	Gastrectomy (n=46)
Type of surgery	
Total gastrectomy	20
Partial gastrectomy	26
Tumor size (mm) largest	83.9
Operation time (minutes)	263
Blood loss (mL)	227
Number of dissected LNs	18.4

DISCUSSION

Two multicenter European RCTs, the Dutch and the MRC trials,[21,22,24] compared D1 and D2 LN dissection. In the Dutch trial which randomized 711 patients (380 to D1 and 331 to D2), the D2 group showed a higher mortality rate (10% vs. 4%, p=0.004), a higher frequency of postoperative complications (43% vs. 25%, p<0.001) and a longer hospital stay (median 25 d vs. 18 d, p<0.001). In 1999 the same authors reported the 5-year survival results: survival rates were similar in the two groups (45% in D1 vs. 47% in D2). The risk of relapse after 5 years was 43% for the D1 group and 37% for the D2 group; the difference suggested only a trend of survival benefit for the D2 group (p=0.22). In 2004 the 11 year follow up also showed: no overall survival benefit with D2 lymphadenectomy (30% with D1 vs. 35% with D2, p=0.53) and only in subgroup analysis patients with N2 disease showed higher survival rate after D2 than after D1procedure. But in 2010 the results of 15-year follow-up showed that D2 lymphadenectomy was associated with lower loco-regional recurrence and gastric-cancer-related death rates, as compared to those of D1 (p=0.01).[23] Subgroup analysis of patients who did not undergo pancreatectomy and splenectomy showed significantly higher overall 15-year survival rate in the D2 group (35% vs. 22%). The authors concluded that, since other studies had recently demonstrated that even in Europe trained surgeons could safely perform D2 lymphadenectomy with spleen and pancreas preservation and that D2 showed more favorable recurrence pattern and cancer-related survival, D2 seemed to be the recommended treatment for patients with resectable gastric cancer. Degiuli et al in 2014 virtually ended the controversy between the East and the West and recommended D2 gastrectomy for all cases of operable gastric cancer. The incidence of malnutrition in patients with advanced Gastric cancer has been shown to be as high as 87%.[25] In a multicenter US Gastric Cancer Collaborative study involving 775 patients undergoing gastrectomy, Ejaz et al observed that BMI <18.5 kg/m^2 and low levels of albumin were related to a significant decrease in overall survival after gastrectomy.[26] In the Indian scenario, 5 studies were considered. In the study conducted by Sunil et al less than 10% of patients had Serum albumin levels less than 3.0 g/dl whereas it was around 78%in our study.[27] Similarly in the retrospective study conducted by Franklyn et al, 26% of included patients had a BMI less than 18.5 whereas it was close to 50% in our study.[28] These significant variations in patient characteristics when compared with other tertiary centres reflects the unfavorable socioeconomic status of the majority of patients who are treated in this hospital.[29,30]

Table 5: Comparative data from other Indian studies.

Percentage	Franklyn et al[28]	Sunil et al[27]	Shrikhande et al[34]	Bhandare et al[36]	Roy et al[35]	Present study
Major morbidity	9.3	5.9	4.4	8.9	22.4	39.1
Mortality	4.2	1.8	1.25	1.5	2.2	6.5

Numerous studies done on malnourished patients undergoing gastrointestinal surgery and gastric cancer surgery in particular concluded that malnourishment portends a poor postoperative course in terms of minor and major morbidity. Mortality risk is also higher in malnourished patients. In this regard D2 gastrectomy with its attendant risk of increased morbidity and mortality poses a formidable challenge.

In the Turkish study postoperative complications in patients treated by D2 gastrectomy occurred in 35% of cases (there was lymphatic leakage resulted from retroperitoneal dissection in 29 patients, wound infection in one patient, anastomotic leakage in one, ileus in two, and nonsurgical complications in six patients. 10.46% of patients who were treated by D2 gastrectomy in Kunisaki et al study had postoperative complications (pulmonary disorders, renal dysfunction, anastomotic leakage, hemorrhage, injury of the biliary tract, pancreatic fistula, wound infection, ileus and heart failure).[29] Significant weight loss is generally seen in patients with incurable solid tumors as observed in our results. Gavazzi et al found weight loss over 5% in the previous three months in 35% of patients recently diagnosed with gastric carcinoma.[30] Rey-Ferro et al found an average of 10% weight loss, and in those who died postoperatively, weight loss had been significantly higher than in those who survived.[31] A major morbidity rate of 39.1% and mortality rate of 6.5% was observed in our study. The morbidity rate following radical gastrectomy is comparable with the morbidity rates in a study conducted in India by Sitaram et al.[32] Three patients died in the 30 day period following surgery. Two patients died due to postoperative pneumonia and one patient died due to complications following massive transfusion in the second post-operative day. Among the 46 patients 20 patients were able to complete cisplatin and 5-fluorouracil adjuvant chemotherapy. Seven patients discontinued chemotherapy due to various reasons. Rest of the patients were lost on follow up. The rate of completion of adjuvant chemotherapy is 43% whereas it is generally found to be around 50% in other studies.[33]

CONCLUSION

D2 gastrectomy for resectable gastric cancer is feasible even in patients who present with advanced disease and malnutrition. The morbidity and mortality rates, though a little higher when compared to other studies from India, is probably due to the unique characteristics of patients like late presentation, advanced nature of the disease and protein calorie malnutrition. Efforts to address the nutritional requirements peri-operatively, combined with radical surgery are the road ahead.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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