

Clinico Pathological Profiles of Patients with Proximal Versus Distal Gastric Adenocarcinoma

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ABSTRACT

One of the most striking epidemiologic observations has been the increasing incidence of adenocarcinomas involving the proximal stomach and distal esophagus. This trend is worrisome, because proximal gastric cancers are thought to have a poorer prognosis, stage, compared with distal cancers. Risk factors are Elevated body mass index, caloric intake, Gastroesophageal reflux disease and smoking. Stomach cancer occurs at a higher incidence in men than in women (ratio of approximately 2:1). The incidence increases with age, peaking in the seventh decade. Comparison of clinicopathological profiles of patients with proximal and distal gastric adenocarcinomas.

Key words: Gastroesophageal, Adenocarcinomas, Distal gastric adenocarcinomas

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INTRODUCTION

Adenocarcinoma of the stomach has been a leading cause of cancer death worldwide through most of the twentieth century. The incidence of this disease has gradually decreased in many parts of the world, due to changes in diet and other environmental factors. With the exception of just a few countries, the prognosis for this disease in the world remains poor. The explanations for these poor results are multifactorial. The lack of well-defined risk factors and specific symptomatology, and the relatively low incidence have contributed to the late stage of onset seen in our country specifically. In Japan, where gastric cancer is endemic, patients are diagnosed at a very early stage, which is reflected in the excellent 50% 5 year survival rate.

Although the incidence of gastric cancer has decreased dramatically over last century, the decline has been limited to cancers below the gastric cardia. The number of newly diagnosed

cases of proximal gastric and gastro-esophageal junction adenocarcinomas has increased markedly since the mid-1980s. The disturbing fact is that these are thought to be biologically more aggressive and more complex to treat than distal tumors [1-35].

MATERIALS AND METHODS

This is a prospective study of patients with Gastric Adenocarcinomas who were admitted in the Department of General Surgery, Sree Balaji Medical College & hospital, Chennai, during the period between July 2016 and July 2018. The patients' history of presenting illness and past history of ulcer treatment as well as gastric surgery was noted. Their personal history was noted, which included their socioeconomic status, habit of smoking, alcohol consumption, diet. The weight and height of all patients were noted to calculate the body mass index (weight in kg / height squared in meters). Their blood groups were noted.

All patients included in this study underwent upper gastrointestinal scopy and an imaging study in the form of a contrast enhanced CT scan of the abdomen. During the endoscopy a

minimum of seven biopsies were taken from the lesion and if an ulcer was found, biopsies around the ulcer crater were taken. Histopathological examination was then performed on the biopsies. Carcinomas of the gastric cardia were defined as: lesions with the center located within 1 cm proximal and 2 cm distal to the esophagogastric junction. According to Siewert: type II was "real" gastric cardia carcinoma and type III was carcinoma located more than 2 cm below the esophagogastric junction (up to a maximum of 5 cm).

Proximal gastric adenocarcinomas included type II tumors, type III tumors, and other tumors up to the distal limit of the proximal third of stomach. The tumors located distal to the limit of the proximal third and up to the pylorus were included as distal gastric adenocarcinomas. All tumors were classified based on intra-operative information or pathology report into different types. The TNM categories were defined based on the 1977 classification, and the residual tumor status -R category, was determined intra-operatively and histopathologically. The standard treatment for proximal gastric carcinoma was total gastrectomy with D2 Lymphadenectomy, omentectomy, with splenectomy. The standard treatment for distal gastric adenocarcinoma was subtotal gastrectomy with D2 lymphadenectomy and omentectomy.

Demographic and clinical variables that are qualitative are given in frequencies with their percentage. Clinical variables which are quantitative are given in mean and standard deviation. Qualitative variables are analyzed using the Pearson chi-square test and Yates corrected Chi square test. Quantitative variables

are analyzed using student independent t-test. P value less than 0.05 are taken as significant.

RESULTS

Patient demographics and history

In our study the male to female ratio was 1.95:1 overall, whereas for proximal tumours it was 1.5:1 and for distal tumors it was 2.12:1 (Figure 1).

Male: Female ratio

In our study the average age of the patients was 57.03 years, with a range of 36 to 72 years. The average age for proximal gastric adenocarcinomas was 53.93 years and for distal gastric adenocarcinomas was 57.98 years; P Value was 0.39, which was not significant (Figure 2).

Body mass index (BMI)

Body mass index was 20.57 overall, whereas it was 20.70 and 20.53 for proximal and distal adenocarcinoma respectively. The P value was 0.93, which was insignificant. Our findings differed from the findings of other studies where proximal tumors were associated with a higher BMI. This is probably because of the small number of patients in our study (Table 1).

Blood group

In our study we did not find any predilection for a particular blood group. P value was 0.21 which was not significant. But it has been proven, persons with blood group A are more at risk gastric adenocarcinomas (Table 2).

Socioeconomic status

In our study 49 patients (75.38%) were from the lower socioeconomic strata. The P value

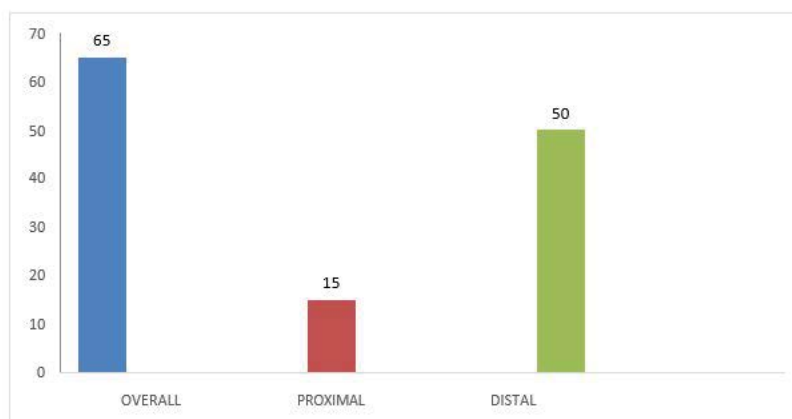


Figure 1: Patient demographics and history.

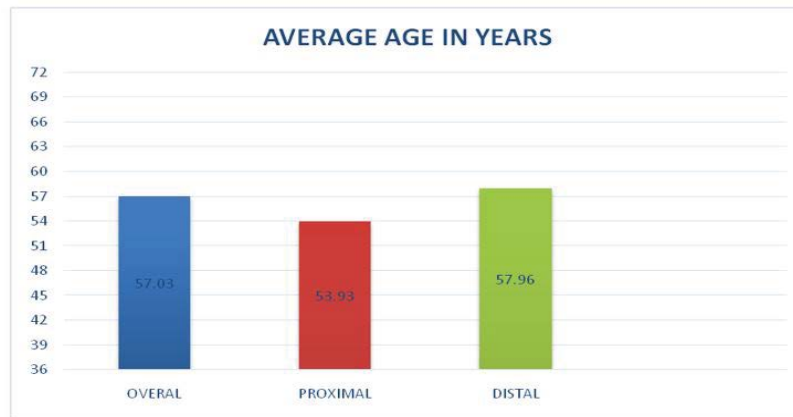


Figure 2: Male: Female ratio.

Table 1: Body mass Index (BMI).

	Overall	Proximal	Distal	Chi-square	P-value
BMI	20.57 ± 6.2	20.7 ± 6.8	20.53 ± 5.0	0.09	0.93

Table 2: Blood group.

Blood group	Overall	Proximal	Distal	Chi-square	P-value
A	14	6	8	4.44	0.21
B	14	2	12		
AB	10	1	9		
O	27	7			

was 0.02, which was significant. This is due to the difficult access to healthcare, more *H. Pylori* infections, lack of knowledge about symptoms, and because our hospital generally attracts and provides healthcare facilities to the poor (Table 3).

Diet

In our study, a higher number of patients (42; 64.61%) consumed a non-vegetarian diet. Vegetarian diet was taken by a smaller percentage (23, 35.38%) of patients, but the difference was not significant, as reflected in the P value of 0.77.

Smoking and alcohol consumption

In our study, 32(49.23%) patients were chronic smokers, and 16 (24.61%) patients were regular alcohol consumers. The P values were 0.71 and 0.89 respectively, which was insignificant.

Previous ulcer treatment

In our study, there were 22 (33.84%) patients who had taken treatment for ulcer before being diagnosed with gastric adenocarcinomas. Out of these, 6 (27.27%) patients had proximal lesions and 16(72.72%) patients had distal lesions. The P value was 0.79 which was not significant (Table 4).

Previous gastric surgery

In our study, 6 (9.2%) patients out of 65 had undergone a gastric surgery previously. The surgery was truncal vagotomy with gastrojejunostomy in all the 6 cases. All 6 patients had distal adenocarcinomas. None of the patients in our study had a family history of gastric cancer.

Clinical presentation symptoms

In our study, 60 (92.30%) patients had dyspepsia; out of this 14 (23.33%) patients had proximal lesions and 46(76.66%) had distal lesions. The P value was 0.70 which was not significant. Out of the 63 (96.92%) patients who had anorexia, 14 (22.22%) patients had proximal lesions and 49(77.77%) patients had distal lesions. The P value was 0.52, which was not significant. In our study weight loss documented in 47 (72.30%) patients overall, 13 (27.65%) of which had proximal lesions, and 34 (72.34%) had distal lesions. The P value was 0.28, which was insignificant. Dysphagia was seen in 12 (18.46%) patients overall; all of who had proximal lesions. This was a very significant finding with P value of 0.001. This finding suggests that proximal lesions present with Dysphagia much more often than the distal tumors do. Persistent vomiting was found in 9 (13.8%) patients overall and all

Table 3: Socioeconomic status.

Socioeconomic status	Overall	Proximal	Distal	Chi-square	P-value
Low	49	9	40	2.52	0.02
Middle	14	4	10		
High	2	2	0		

Table 4: Previous ulcer treatment.

Ulcer treatment	Overall	Proximal	Distal	Chi-square	P-value
Ulcer treatment	22	6	16	0.07	0.79

these patients had distal lesions, despite which the P value was 0.18. This was not significant. 31 (47.69%) of the patients presented with melena as a symptom. Out of these 4 (12.9%) had proximal lesions, and 27 (87.09%) had distal lesions which was not significant statistically (P value-0.12). Jaundice was seen in two patients one each from either group (Table 5).

Signs

In our study, 44(67.69%) patients had anemia, out of which 10 (22.72%) had proximal lesions and 34 (77.27%) had distal lesions. P value was insignificant at 0.92. Mass abdomen was found in 26 (40%) of the patients overall, of which 7 (26.92%) had proximal tumors and 19 (73.07%) had distal tumors. P value was 0.54, which was not significant. In our study, Hepatomegaly was found in 10 (15.38%) patients, 5 (50%) of these patients had proximal adenocarcinomas and 5 (50%) had distal tumors. P value was found to be 0.03, which was significant. This implies that proximal tumors have Hepatomegaly more often than the distal tumors. In our study, ascites was found in 7 patients overall and supraclavicular nodes were found in 6 patients overall. The difference in the incidence of these signs between proximal and distal tumors was not significant statistically (Table 6).

Upper gastrointestinal endoscopy

In our study, we found that the average size of the tumor was 3.67 cm overall, with a range of 2.5 cm to 6.0 cm. In proximal tumors, the average size was 3.70 cm, while in distal tumors it was 3.67 cm (Table 7 and Figure 3).

Out of the 65 patients studied, 15 (23.07%) patients had proximal tumors and 50 (76.92%) patients had distal tumors. This finding implies that the incidence of proximal gastric adenocarcinomas is not increasing in our population, whereas in the Western hemisphere there is an alarming rise in proximal gastric

adenocarcinomas to an extent that these tumors from about 45% of the total gastric adenocarcinomas (Figure 4).

The morphology of the tumor on upper GI scopy was described as ulcerating, polypoid or superficial. Overall 21 (32.30%) were ulcerating growths; of which 2 (9.5%) were located proximally and 19 (90.47%) were located distally. 33 (50.76%) were polypoid growths, of which 12 (36.36%) were located proximally, and 21 (63.63%) were located distally. Out of the 11 (16.92%) superficial growths 1 (9.09%) was located proximally and 10 (90.90%) were distal growths. The P value was 0.03 which was significant (Table 8).

Distensibility of the stomach was decreased in 18 (27.69%) patients. Out of these 2 (11.11%) were in patients with proximal lesions, and 16 (88.88%) were in patients with distal tumors. The difference was not statistically significant with a P value of 0.27. Abnormal *pyloric* function was found in 11 (16.92%) of the patients overall and all these patients had distal lesions. P value was significant at 0.05.

On histopathological examination the tumors were classified into well, moderately, and poorly differentiated adenocarcinoma. Out of the 17 (26.15%) well-differentiated tumors, 4 (23.52%) were located proximally and 13 (76.47%) located distally. Moderate differentiation was seen in 26 (40%) of the total lesions; of which 7 (26.92%) were proximal and 19 (73.07%) were distal. Poorly differentiated tumors were seen in 22 (33.84%) of the total; out of these 4 (18.18%) were proximal and 18 (81.81%) were distal tumors. The P value was not significant (Table 9).

Histopathology

The tumors were classified as either intestinal type or diffuse type according to Lauren classification. The intestinal type were 42

Table 5: Previous gastric surgery.

	Overall	Proximal	Distal	Chi-square	P-value
Dyspepsia	60	14	46	0.15	0.7
Anorexia	63	14	49	0.4	0.52
Weight loss	47	13	34	1.18	0.28
Dysphagia	12	12	0	43.8	0.001
Vomiting	9	0	9	1.81	0.18
Malena	31	4	27	2.45	0.12
Jaundice	2	1	1	0	1

Table 6: Signs.

	Overall	Proximal	Distal	Chi-square	P-value
Anemia	44	10	34	0.05	0.92
Mass abdomen	26	7	19	0.36	0.54
Hepatomegaly	10	5	5	4.83	0.03
Ascites	7	2	5	0.01	0.91
Supraclavicularnode	6	0	6	0.18	0.36

Table 7: Upper gastrointestinal endoscopy.

	Total	Proximal	Distal
Size (in cm)	3.67	3.7	3.67
Location	65	15	50

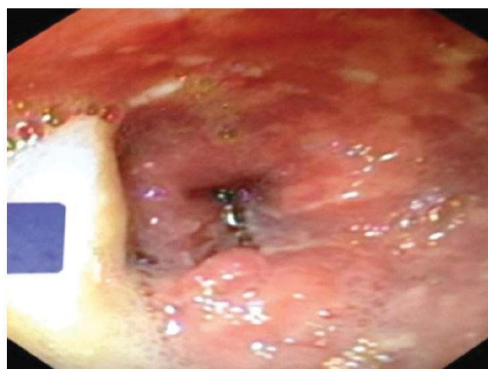


Figure 3: Antral carcinoma endoscopic view.



Figure 4: Adenocarcinoma of lesser curvature endoscopic view.

Table 8: Morphology of the tumor on upper GI scopy.

	Overall	Proximal	Distal	Chi-square	P-value
Ulcerating	21	2	19	6.67	0.03
Polypoid	33	12	21		
Superficial	11	1	10		
Decreased distensibility of stomach	18	2	16	1.18	0.27
Abnormal <i>pyloric</i> function	11	0	11	3.97	0.05

(64.61%) overall; of which 13 (30.95%) were proximal tumors and 29 (69.04%) were distal. 13 out of the 15 proximal lesions (86.66%), were of the intestinal type. The P value (0.04) was significant. The diffuse type was 23 (35.38%) overall; of which 2 (8.6%) were proximal tumors and 21 (91.30%) were distal. The P value (0.04) was significant (Table 10).

Staging

There was no significant difference between the proximal and distal gastric adenocarcinomas when all the stages were considered together, the chi-square being 3.99 and p value being 0.26. But when stage III and IV was considered alone, it was found that more number of proximal tumors had presented at a later stage than the distal tumors (Table 11).

Hepatic metastasis (H)

Hepatic deposits were found in 17 (26.15%) patients overall. Of these 7 (41.17%) were due

to proximal tumors and 10 (58.82%)n were due to distal tumors. The P value was 0.04 which was significant (Table 12 and Figure 5).

Peritoneal metastasis (P)

In our study, peritoneal metastases were found in 9 (13.84%) patients overall. Out of these 4 (44.4%) were due to proximal tumors, and 5 (55.55%) were due to distal tumors. The P value was 0.22, which was insignificant (Table 13).

CONCLUSION

In our study, there was no difference in the degree of differentiation between the proximal and the distal tumors. The proximal tumors were more often of the intestinal type when compared to the distal tumors, which was statistically significant. This was also in accordance with the findings in other studies. Proximal tumors tend to present at a higher stage than the distal tumors. But this was not statistically significant. Proximal tumors

Table 9: Histopathological examination.

Differentiation	Overall	Proximal	Distal	Chi-square	P value
Well	17	4	13	0.04	0.95
Moderate	26	7	19	0.36	0.55
Poor	22	4	18	0.13	0.72

Table 10: Histopathology.

Lauren classification	Overall	Proximal	Distal	Chi-square	P-value
Intestinal	42	13	29	4.15	0.04
Diffuse	23	2	21	4.15	0.04

Table 11: Staging.

	Overall	Proximal	Distal
I A	0	0	0
I B	6	0	6
II	13	3	10
III	17	1	16
III B	6	3	3
IV	23	8	15

Table 12: Hepatic metastasis (H).

	Overall	Proximal	Distal	Chi-square	P-value
H	17	7	10	4.25	0.04

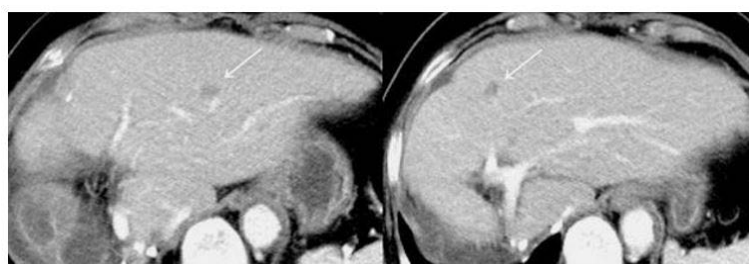


Figure 5: CT image showing liver metastasis.

Table 13: Peritoneal metastasis (P).

	Overall	Proximal	Distal	Chi-square	P value
P	9	4	5	1.47	0.22

have hepatic metastasis at presentation more frequently than the distal tumors, which was a statistically significant finding in our study.

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ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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