

Original Research Article**A Retrospective Study to Find Correlation Between Clinical and Pathological Factors of Gastric Cancer****Sujeet Kumar Mandal¹, Pankaj Kumar Suman²****¹Assistant Professor, Department of Pathology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India****²Tutor, Department of Pathology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India**

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Abstract

Aim: The aim of this study was to find correlation between clinical and pathological factors of gastric cancer in Bihar region, India. **Methods:** This retrospective study was carried out in the Department of Pathology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India, for 1 year. **Results:** Of these 80 patients, 50(62.5%) male and 30 (37.5%) female, 50(62.5%) underwent distal gastrectomy, 5 (6.25%) proximal gastrectomy via abdomen and 15 (18.75%) via thorax, and 10(12.5%) underwent total gastrectomy. Distal and total gastrectomy had more numbers of clearances of lymph nodes than the other operational approaches. The postoperative complications occurred in 8 patients, 10%, including gastric retention in 20(25%), anastomotic leakage in 10(12.5%), infection of incision in 9(11.25%), disruption of wound in 5(6.25%), and thoracic cavity effusion in 5(6.25%). The complication was most common in proximal gastrectomy via abdomen (30% patients). The overall mortality was 1.25% (1/80). The diameter of the neoplasm was positively correlated with the depth of infiltration and lymphatic metastasis rate while hemoglobin was the opposite. 12(15%) of 80 were early gastric carcinoma (EGC) with metastasis of lymph nodes in 12 patients (15%). The frequency of positive lymph nodes in these patients was 4%-5% less than in advanced gastric cancer (Table 2). In linear regression analysis, age and diameter of the tumor were negatively correlated with the preoperative hemoglobin ($P < 0.001$). The diameter of the tumor was positively correlated with age and the frequency of positive lymph nodes ($P < 0.01$). The patients with tumor of bad differentiation were younger than the other groups, who had larger tumor diameter and higher frequency of positive lymph nodes. The degree of differentiation was not related with the depth of tumor invasion on the gastric wall. The tumor diameter on the corpus and fundus was larger than the others, which had higher frequency of positive lymph nodes. The proximal gastric cancer, bad differentiation and frequency $>36%$ positive lymph nodes were more common in female than in male. **Conclusion:** This retrospective study has shown that clinic-pathological characters in gastric cancer varied with sex, location, and diameter of the tumor.

Keywords: Gastric Cancer, Proliferative, Apoptotic.

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Introduction

Gastric cancer is a heterogeneous, multifactorial disease, which is known as the fifth most common cancer and the third leading cause of cancer-related death worldwide in 2018[1,2]. Increased understanding of the proliferative and apoptotic changes in gastric cancer, particularly the identification of novel biomarkers for cancer diagnosis and targets for treatment, may result in the improvement of diagnosis, treatment and prevention. According to previous reports, ~0.7million people died because of gastric cancer each year[3] and about 70% of the gastric cancer cases had high fatality, significantly higher than other cancers such as the liver and breast cancers[4]. However, the incidence and mortality of gastric carcinoma vary geographically; they were dramatically different between Western and Eastern countries[3]. The epidemiological and clinic-pathological characteristics of gastric cancer still largely remain uncertain, although some risk factors have been identified in the study. It has been reported that the survival rates were lower among smokers, alcohol drinkers, obesity and people who have the symptom of esophageal acid reflux and consume pickled, salty and smoked food[5-6]. Studies also suggested that the incidence rate of gastric cancer was highly correlated with age, especially among patients aged between 50 and 70 years old[7-8]. It has been reported that gastric carcinoma is one of the heaviest burdens of cancer-related cost, the absolute numbers of gastric cancer cases and the prognosis remain big issues in the health programmes[9].

The current most popular therapy for gastric cancer is surgery combined with chemotherapy. Surgery is the most preferred treatment for gastric carcinoma, but the survival rate of patients undergoing surgery remains very low. Previous studies have revealed that the average survival time of patients with advanced gastric cancer is <12 months[10,11]. Therefore, how to timely assess the condition, judge the prognosis risk after therapy and develop a reasonable postoperative care programme becomes a vital part of gastric cancer treatment[12,13]. Many clinic-pathological factors, including clinical stage, tumour size, infiltration depth, Lauren classification and lymph node metastasis rate, might jointly influence the prognosis in patients with gastric carcinoma[14,15]. It is important but challenging to identify the most significant and independent factors associated with prognosis since many factors are highly correlated. To have a systematic comprehension of gastric carcinoma and to identify independent risk factors on gastric cancer patients, we conducted the current study.

Material and methods

This retrospective study was carried out in the Department of Pathology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India, for 1 year, after taking the approval of the protocol review committee and institutional ethics committee. Total 80 patients were included in this study.

We analyzed the following clinic pathologic and surgical factors: age, sex, hemoglobin, operation manners, operation time, and amount of transfusion during operation, postoperative hospital stay, postoperative complications, positive proximal margin, location of tumor, tumor size, differentiation, depth of tumor invasion, lymph nodes and lymphatic metastasis rate.

Frequency of positive lymph nodes = numbers of metastatic lymph nodes / all lymph nodes excised \times 100%.

Results

Of these 80 patients, 50(62.5%) male and 30 (37.5%) female, 50(62.5%) underwent distal gastrectomy, 5 (6.25%) proximal gastrectomy via abdomen and 15 (18.75%) via thorax, and 10(12.5%) underwent total gastrectomy. Distal and total gastrectomy had more numbers of clearances of lymph nodes than the other operational approaches. The postoperative complications occurred in 8 patients, 10%, including gastric retention in 20(25%), anastomotic leakage in 10(12.5%), infection of incision in 9(11.25%), disruption of wound in 5(6.25%), and thoracic cavity effusion in 5(6.25%). The complication was most common in proximal gastrectomy via abdomen (30% patients) (Table1). The overall mortality was 1.25% (1/80).

The diameter of the neoplasm was positively correlated with the depth of infiltration and lymphatic metastasis rate while hemoglobin was the opposite. 12(15%) of 80 were early gastric carcinoma (EGC) with metastasis of lymph nodes in 12 patients (15%). The frequency of positive lymph nodes in these patients was 4%-5% less than in advanced gastric cancer (Table 2). In linear regression analysis, age and diameter of the tumor were negatively correlated with the preoperative hemoglobin ($P<0.001$). The diameter of the tumor was positively correlated with age and the frequency of positive lymph nodes ($P<0.01$).

The patients with tumor of bad differentiation were younger than the other groups, who had larger tumor diameter and higher frequency of positive lymph nodes. The degree of differentiation was not related with the depth of tumor invasion on the gastric wall (Table 3). The tumor diameter on the corpus and fundus was larger than the others, which had higher frequency of positive lymph nodes (Table 4). The proximal gastric cancer, bad differentiation and frequency $>36\%$ positive lymph nodes were more common in female than in male (Table5).

Multiple analysis demonstrated that sex, location of tumor, tumor diameter, depth of tumor invasion and differentiation play an important role in the metastasis of lymph nodes (Table 6).

Table 1: Comparison of operation manner with numbers of lymph nodes, time for operation, amount of blood transfusion during operation, hospitalization days and complications ($\bar{x} \pm s_x$)

Manners of operation	N (80)	Numbers lymph nodes	Time for operation (hours)	Amount of blood transfusion (mL)	Hospitalization stays (days)	Complication (%)
Distal gastrectomy	50	11.1±0.2*	3.7±0.04	402.65±14.77*	15.8±0.54	8.5
Proximal gastrectomy via abdomen	5	8.2 ±0.52	4.32±0.1*	609.36±40.39*	17.8±1.5	14*
Proximal gastrectomy via thorax	15	8.5±0.6	3.35±0.01	749.21±17.98	14.8±0.6	1.7
Total gastrectomy	10	13.2±0.2*	4.55±0.3*	747.03±44.69	19.1±1.3	12.1
P		<0.0001	<0.0001	<0.0001	>0.05	<0.001

*Compared with other operative approaches

Table 2: Comparison of depth of infiltration with age, diameter, hemoglobin, and lymphatic metastasis rate ($\bar{x} \pm s_x$)

Depth of invasion	N (80)	Age (yrs)	Diameter (cm)	Hemoglobin(g/L)	Lymphatic metastasis rate (%)
pT1(m)	14	52.1 ±1.7	2.38 ± 0.3	12.33 ± 0.5	3.17 ± 0.5
pT1(ms)	7	56.2±1.3*	2.58 ± 0.6	11.77± 0.4*	4.27 ± 1.0
pT2	8	56.9±1.4*	2.96 ± 0.5	11.87 ± 0.3*	8.73 ± 1.3*
pT3	9	57.6±1.3*	4.32 ± 0.4*	11.85 ± 0.3*	18.31 ± 2.5*
pT4	42	58.5±0.2*	5.42 ± 0.2*	11.64 ± 0.3*	34.52 ± 1.4*
P		<0.003	<0.0001	<0.001	<0.0001

Compared with pT1 (m).

Table 3: Comparison of differentiation with age, diameter, hemoglobin and lymphatic metastasis rate ($\bar{x} \pm s_x$)

Differentiation	N (80)	Age (yrs)	Diameter (cm)	Hemoglobin (g/L)	Lymphatic metastasis rate (%)
I	7	60.9±1.3	3.43±0.4	10.7±0.5	10.4±3.2*
II	10	59.9±0.5	3.97±0.5	11.6±0.3	24.2±2.2
III	26	60.1±0.3	4.20±0.2	11.3±0.5	20.9±1.5
IV	37	54.1±0.3*	4.82±0.1*	11.6±0.1*	30.9±1.3*
P		< 0.0001	= 0.002	= 0.01	< 0.0001

*Compared with other groups

Table 4: Comparison of tumor site with age, diameter, hemoglobin and positive lymph node rate ($\bar{x} \pm s_x$)

Location of tumor	N (80)	Age (yrs)	Diameter (cm)	Hemoglobin (g / L)	Lymphatic metastasis rate (%)
Pylorus	10	54.1±2.1	3.5±0.6	12.9±0.8	13.77±3.2
Antrum	12	57.1±0.4*	4.6±0.4	12.6±0.5	25.65±1.4
Incisura	8	56.1±0.3	3.3±0.3	12.6±0.2	20.36±1.5
Corpus	10	57.2±1.2	5.6±0.3*	11.4±0.3	35.77±3.8*
Fundus	13	59.7±0.4*	5.3±0.2*	12.6±0.3	33.88±1.8*
<i>P</i>		< 0.0001	< 0.0001	> 0.005	< 0.001

*Compared with other locations.

Table 5: Comparison of sex with tumor location, differentiation, depth of invasion and positive lymph node rate ($\bar{x} \pm s_x$)

Gender	Location (%)			Differentiation (%)			Depth of invasion (%)			Frequency of metastatic lymph node (%)	
	Proximal	Middle	Distal	Well	Middle	bad	pT1	pT2	pT3	<35	>35
Male =50	4	3	3	2	3	4	2	4	10	8	7
Female =30	2	1	2	3	2	6	2	1	5	4	2
		<0.001	<0.001					>0.05	=0.01	<0.001	

Table 6: Multi-factors analysis of lymphatic metastasis in gastric patients

Related factors	Regression coefficient	Standard error	Standard regression coefficient	<i>P</i>
Constant	-22.4	7.5		0.001
Age	-0.0081	0.085	-0.27	0.412
Sex	-6.642	2.051	-0.077	0.001
Tumor location	2.425	0.692	0.074	0.003
Diameter of tumor	2.465	0.528	0.152	0.0001
Depth of invasion	7.231	0.775	0.279	0.0001
Differentiation	3.695	1.136	0.087	0.001

Discussion

Gastric cancer remains one of most common causes of death. Although the etiology of gastric cancer is still unclear, but studies have shown that many factors are associated with the development, metastasis of gastric cancer, and recurrence

after operation[16-18]. Recent studies suggest that infection with *Helicobacter pylori* may play an important role in the development of gastric cancer[19,20]. It has been proposed that *Helicobacter pylori* infection may produce acute and chronic gastritis, intestinal metaplasia, dysplasia, and eventually resulting in gastric cancer.

Some abnormal expression[21,22] in gene is involved in carcinogenesis of gastric cancer such as matrix metalloproteinases gene, p53 gene and dinucleotide repeat sequence gene. Abnormal contents of some trace elements may also be one of the risk factors in gastric cancer[23,24]. Early gastric cancer (EGC) has been considered to be a form of gastric malignancy with a relatively good long-term prognosis compared to that of advanced gastric cancer because of rare metastasis in lymph nodes[25,26]. In Japan, EGC is diagnosed in 30%-50%, due to partly at least the extensive use of endoscopy and mass screening programs[27,28]. In this study, the proportion of EGC diagnosed in all patients is 65(16.25%) similar to the proportion in the United States and Europe[29,30]. In recent years, endoscopic treatment has become increasingly popular as an alternative to surgical treatment of patients with EGC in hope of offering superior quality of life (QOL)[31]. However, because of presence of metastasis in 10%-20% and skip metastasis of lymph nodes, whether the rationale for a standard resection with systematic lymphadenectomy is necessary is still a controversial issue[32].

Different operative approaches were carried out according to the different locations of the tumor. In our study, the number of lymph nodes excised was the largest in total gastrectomy, followed by distal gastrectomy which may be related to the resection of all or most parts of omentum. The number of lymph nodes excised in proximal gastrectomy via a trans abdomen was similar to via transthorax. There was shorter time for operation and lower frequency of complication in proximal gastrectomy via trans thorax while lower blood transfusion in proximal gastrectomy via trans abdomen. The postoperative hospitalization stays and the positive resection margin was same between them. The complications varied

among different operations: gastric retention was common in distal gastrectomy while thorax effusion and infection of lung were mainly found in total gastrectomy.

Although the overall incidence of gastric cancer has remained stable in the West, there is well- documented shift from distal to proximal lesion. The clinical relevance of this shift is that the overall prognosis for patients with proximal gastric cancer is worse than for those with distal tumor. This difference in survival may be attributed to a variety of factors, ranging from an increased biologic aggressiveness of proximal tumors to an advanced stage of presentation[33,34]. In study, a higher frequency of positive lymph nodes was found in gastric cancer located on corpus and the fundus which may be associated with the larger diameter of the tumor in corpus and the fundus. In tumors with larger diameters there were worse differentiation, deeper infiltration, and higher frequency of positive lymph nodes. Apparently, the prognosis will be worse in these patients. The present results also show that the more proximal lesions, bad differentiation, and the higher >35% frequency of positive lymph nodes can be found in female than in male. The numbers of metastatic lymph nodes play an important role in the long-term outcome after curative resection[35,36]. Thus it is suggested that extended lymphadenectomy should be performed in advanced gastric cancer[37]. Our multivariate analysis indicated that among six clinicopathologic variables (age, sex, location of tumor, tumor diameter, depth of invasion and differentiation), the depth of invasion was the most important factor influencing metastasis of lymph node.

Conclusion

This retrospective study has shown that clinic-pathological characters in gastric cancer varied with sex, location, and diameter of the tumor. The depth of

invasion plays a very important role in metastasis of lymph node. The prognosis in female with gastric cancer may be worse than in man. Because metastasis of lymph nodes may occur even in patients with EGC, radical gastrectomy with lymphadenectomy may be necessary in all stages of gastric cancer.

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