# Current Status of Gastric Cancer in Thai Patients

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**Abstract**

To determine the current status in various aspects of gastric cancer in Thai patients, we retrospectively reviewed the records of 119 patients with histologically proven gastric cancer in King Chulalongkorn Memorial Hospital during the five-year period from 1994 to 1998. There were 72 males (60.5%) and 47 females (39.5%) with ages ranging from 22 to 91 years (mean age 60.2±15.1 years). Among these, 20 patients (16.8%) were younger than 40 years. The duration of symptoms prior to first presentation averaged 20 weeks and dyspepsia and weight loss were the most common complaints. Lesion location was lower third in 40.3 per cent, middle third in 31.9 per cent, upper third in 15.1 per cent and entire stomach in 3.4 per cent of patients. Adenocarcinoma was the most common histological finding (91.6%), followed by lymphoma and leiomyosarcoma (3.4% each). *Helicobacter pylori* infection was detected in 17 of 25 (68%). The TMN staging was as follows: stage II, 5.9 per cent; stage III, 9.2 per cent; and stage IV, 68.9 per cent. (the stage was unknown in 16%). The overall 1-year, 2-year and 5-year survival rates were 51.6 per cent, 17.5 per cent and 4.4 per cent, respectively. Management was surgical treatment in 58.9 per cent (total gastrectomy 14.5%, subtotal gastrectomy 33.3% and palliative bypass surgery in 11.1%). Systemic chemotherapy was the primary modality of therapy in 16.8 per cent and was adjuvant therapy in 18.5 per cent. The median survival time of resectable cases was 1.00±0.53 years, significantly longer than that of unresectable cases (0.11±0.03 years) ($p=0.0025$). However, the administration of chemotherapy did not improve the survival rate. It is concluded that, in Thailand, gastric cancer continues to be an important health problem and is generally associated with a poor prognosis.

**Key word** : Gastric Cancer, Thai Patients

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Gastric carcinoma is one of the most common malignant diseases worldwide[1]. Although its incidence has declined dramatically in the United States and Western Europe over the past 60 years, in developing countries the incidence remains very high[2]. The factors leading to this variability among countries are still not clear. Some correlation exists between the occurrence of gastric carcinoma and the prevalence of *Helicobacter pylori* infection in different geographical areas[3]. However, a high prevalence of *H. pylori* gastritis does not necessarily predict a high prevalence of gastric cancer. Recent data indicate that exposure to environmental factors other than *H. pylori* such as dietary factors, as well as host genetic alterations are important in the evolution of gastric cancer [4,5].

In Thailand, as in other developing countries, gastric cancer remains one of the most frequent cancers in both sexes and accounts for 1-2 percent of all incident cancers[6]. We therefore undertook a retrospective study with the following aims: 1) to assess the clinical data of gastric cancer among Thai patients, and 2) to assess the clinical outcome and prognostic factors of survival.

## MATERIAL AND METHOD

A retrospective study of medical records of all patients with histologically proven gastric cancers between January 1994 and December 1998 at King Chulalongkorn Memorial Hospital was performed. The charts of the patients were analyzed to ascertain the clinical information. Endoscopy reports were reviewed to assess the location and characteristics of the tumor. Furthermore, radiology reports were used to assess the extent of the primary tumor, as well as the presence of distant metastases. Pathology results from either endoscopic biopsy or surgical specimens were examined for the type and pathologic stage of the tumor. In addition, the prevalence of *H. pylori* infection among these patients was demonstrated. Descriptive statistics calculated the patients' characteristics and independent *t*-test was used to assess group differences. Survival data were analyzed according to the method of Kaplan and Meier for incomplete observations. For the calculation of statistical differences concerning survival data, the Log Rank test was applied. Statistical significance was defined as $p< 0.05$.

## RESULTS

Between January 1994 and December 1998, 119 patients with gastric cancer were identified. There were 72 males (60.5%) and 47 females (39.5%) with ages ranging from 22 to 91 years (mean age 60.2±15.1 years) (Fig. 1). The effect of age was similar for both sexes, with a slight increase in the sixth and seventh decades. However, there were 20 patients (16.8%) younger than 40 years in our series. Only 32 patients (26.9%) were smokers, while 21 patients (17.6%) were heavy alcoholic drinkers. Among these, there were 14 patients who had a history of both smoking and heavy drinking. In our study, only one patient had a family history of gastric cancer.

The mean length of disease history prior to diagnosis was 20 weeks. The most common symptoms observed were dyspepsia (61.3%), following by significant weight loss and anorexia in 53.8 per cent and 31.1 per cent of the cases, respectively (Table 1). Interestingly, malignant ascites were found in a higher proportion among the younger patients (<40 years) than the older ones (35.3% and 10.9%, respectively, $p=0.017$).

It was possible to assess the primary tumor site in 108 cases (90.8%). The lower third (the pylorus and antrum) was involved by cancer in 40.3 per cent. Whereas, the middle third (greater and lesser curvature of the corpus) and upper third (the fundus and cardia) were involved in 31.9 per cent and 15.1 per cent, respectively. The entire stomach was cancerous (diffuse infiltration) in the remaining 3.4 per cent. (Table 2). Regarding endoscopic features of gastric cancer, several appearances were identified including ulceration (67.9%), polypoid mass (24.4%), linitis plastica (3.4%) and submucosal lesion (0.8%). The average size of tumor ulceration and mass was 5.2±2.4 cm. Histologically, more than 90 per cent of cases in our series were adenocarcinoma, and the remainder were lymphoma (3.4%), leiomyosarcoma (3.4%), metastatic malignant melanoma (0.8%) and undifferentiated carcinoma (0.8%).

Regarding *Helicobacter pylori* infection, the results of CLO®test for this bacterium were available in only 25 cases, seventeen of which were positive (68%), whereas, 8 were negative (32%). Concerning tumor markers of gastric cancer, the serum CA 19-9 was elevated in 13 of 15 (86.7%) and serum carcinoembryonic antigen (CEA) eleva-

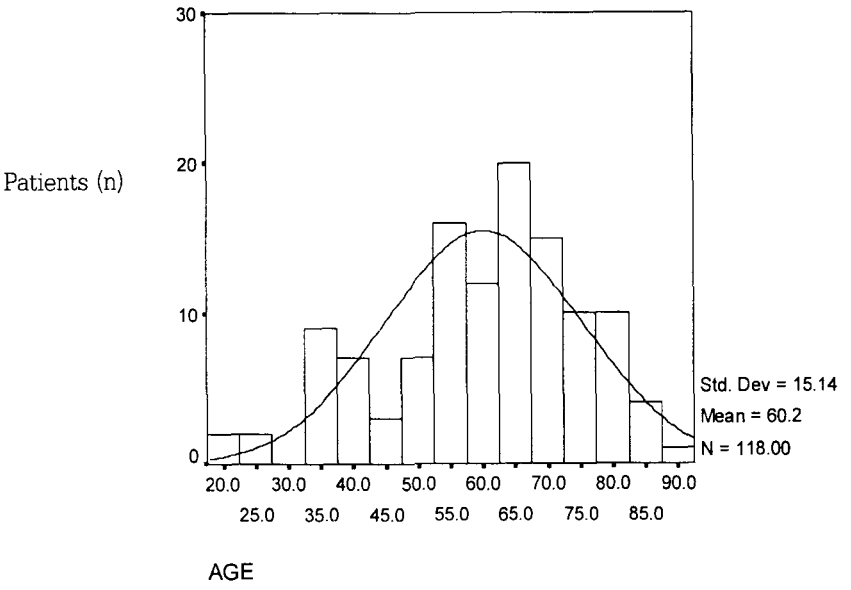


**Fig. 1. Age distribution of the patients.**

**Table 1. Symptoms and signs present at initial diagnosis.**

| Symptoms & signs | Number of patients | Percentage |
|---|---|---|
| Dyspepsia | 73 | 61.3 |
| Weight loss | 64 | 53.8 |
| Anorexia | 37 | 31.1 |
| Upper GI bleeding | 34 | 28.6 |
| Gastric outlet obstruction | 25 | 21.0 |
| Ascites | 17 | 14.3 |
| Abdominal mass | 14 | 11.8 |
| Dysphagia | 8 | 6.7 |
| Fatigue | 7 | 5.9 |
| Prolonged fever | 2 | 1.7 |
| Gastric perforation | 2 | 1.7 |

**Table 2. Tumor site within the stomach.**

| Site | Number of patients | Percentage |
|---|---|---|
| Pyloric-antrum | 48 | 40.3 |
| Greater curve of body | 25 | 21.0 |
| Lesser curve of body | 13 | 10.9 |
| Cardia | 12 | 10.1 |
| Fundus | 6 | 5.0 |
| Diffuse infiltration | 4 | 3.4 |
| Unknown | 11 | 9.2 |
| Total | 119 | 100 |

tion was noted in 9 of 30 cases (30%). The alpha-fetoprotein (AFP) level, a marker more commonly used for hepatocellular carcinoma, was elevated in only 2 of 19 cases (10.5%).

The tumor staging according to the TMN classification at the time of diagnosis was as follows: 7 (5.9%) were classified as stage II, 11 (9.2%) as stage III, and 82 (68.9%) as stage IV; the stage was unknown in 19 (16%) of the cases. For the advanced stage, lymph node metastasis was found in 36.4 per cent, liver metastasis in 19.6 per cent peritoneal metastasis in 21.5 per cent and the remainder involved the bone, lung or adjacent organs.

Management was primarily surgical resection in 56 (47.8%) and was complemented by systemic chemotherapy in 22 (18.5%) of the cases. The type of surgery varied according to the location and extent of the tumor. Total gastrectomy was performed in 14.5 per cent and subtotal gastrectomy was performed in 33.3 per cent. Surgical exploration with only palliative bypass surgery

was performed in 11.1 per cent. The median survival time of resectable cases was 1.00±0.53 years (95% CI was 0.57, 2.66), which was significantly longer than that of unresectable cases (0.11±0.03 years, 95% CI was 0.05, 0.17) ($p=0.0025$). In addition, systemic chemotherapy was the primary modality of therapy in 20 (16.8%) of the cases. However, the administration of chemotherapy did not lead to an increased rate of survival when compared to supportive treatment alone. ($p>0.05$). The overall 1-year, 2-year and 5-year survival rates were 51.6 per cent, 17.5 per cent and 4.4 per cent, respectively (Fig. 2). Another prognostic factor in our study was serum albumin level at initial diagnosis. As shown in Fig. 3, the median survival time was reduced with a decrease in serum albumin

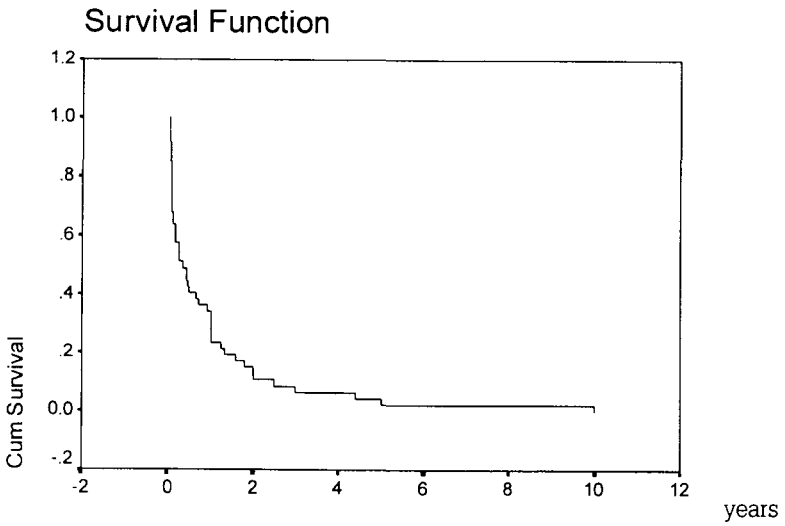


**Fig. 2. Survival analysis of the patients.**

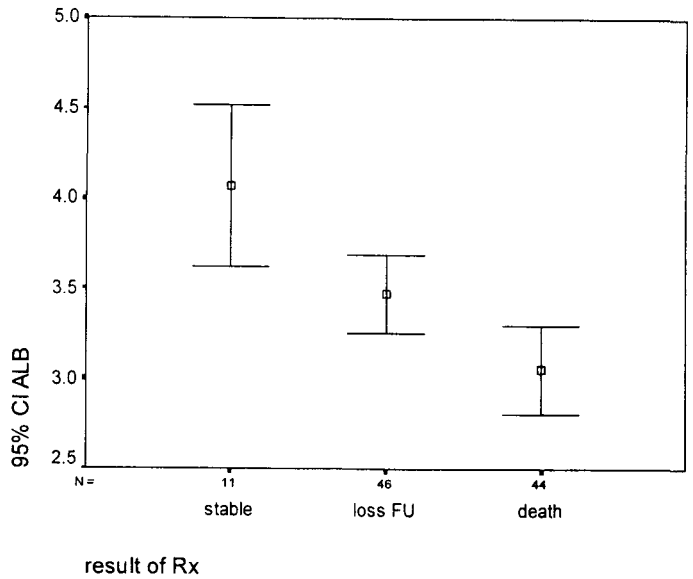


**Fig. 3. Comparison of the albumin level in various groups of patients at initial diagnosis.**

level. On the other hand, the patients' age, sex, levels of CEA and CA 19-9, level of hematocrit and tumor size had little influence on the survival time.

## DISCUSSION

This study presents a broad picture of various aspects of gastric cancer in Thai patients. We point out that our study was limited to a retrospective review of patients' medical records. However, through the data available, it was possible to assess these patients' collective and therapeutic results and to make a comparison between Thai patients and Western, as well as Japanese patients.

As with many malignancies, gastric cancer is a disease of middle and old age with male preponderance regardless of high- and low-risk countries. In our study, as shown in Fig. 1, it peaked within the age group of 55 to 70 years (32). The ratio between male to female was 1.53 : 1. Although it predominately affected the older age group, a significant proportion, approximately one-fifth, in our series were younger than 40 years at the time of diagnosis. In general, gastric cancer in young patients is more likely to be of the diffuse type and associated with a poorer prognosis(7,8). Similarly, among young patients in this study, it appeared that the cancer had an increased tendency to have distance metastasis, particularly to the peritoneum. It should also be mentioned that younger patients tended to have their diagnoses delayed, probably due to the misconception of physicians that they were dealing with a benign process.

Considerable evidence suggests that exposure to environmental factors early in life contribute to the development of gastric cancer, with diet the most likely cause(1). In addition, previous studies have found that cigarette smoking is a risk factor for this cancer. Nonetheless, most have failed to demonstrate a clear dose-response relationship(9,10). Moreover, one study found that only when smoking was combined with alcohol was there a significant risk factor for gastric cancer, whereas, alcohol consumption per se had no such effect(11). These findings have led to the hypothesis that smokers share a common risk factor that increases their risk to gastric cancer, but is independent of the effects of the cigarette. In our population, we could find only a small percentage of cases who were smokers and/or drinkers.

Dyspepsia and weight loss were the most frequent initial symptoms in our series, corresponding to Western studies(12,13,31). Furthermore, the average time from developing symptoms to seeing a physician was comparable to most series(12,14,15). However, we could detect a high proportion of patients presenting with either gastric outlet obstruction, indicating large tumors located near the pylorus, or malignant ascites associated with the implant of tumor cells in the peritoneal cavity. Factors contribute to this high frequency of advanced gastric cancer at initial diagnosis not only from its nonspecific manifestations early in its course, but could also be from a tendency towards self-treated attitude until advanced stage in some cases.

The classification of gastric adenocarcinoma into the intestinal type and diffuse type has been shown to be valuable for epidemiologic studies, as well as the prognosis of this cancer. The intestinal type tends to predominate in areas with a high incidence of the cancer, whereas, the incidence of diffuse-type lesions is similar in most countries throughout the world(16). Diffuse carcinomas occur more often in young patients and are associated with a worse prognosis(1). From a previous review in our hospital(17), approximately fifty-six per cent of gastric cancer was classified as an intestinal type and the remaining as a diffuse type. There were no significant differences in the age distribution with regard to different tumor types, however, the intestinal type was proportionately more common in men. Moreover, there was no significant association between *H. pylori* infection and histological type of the tumor. These findings differed from most reports from Japan and Western countries, in which the infection is largely restricted to intestinal-type cancers(18,19).

In terms of tumor location, our study demonstrated that any area of the stomach can be involved predominantly in the distal part and on the descent towards the proximal part of the stomach. However, it is noteworthy that there has been an unexplained steady rise in the incidence of gastric cancer in the proximal third over the past decades in Western countries(20). Whether there is such a change in location among Thai patients, is certainly a subject of interest in the future.

Regarding *H. pylori* infection, epidemiological studies were the first to demonstrate the important association between the infection and gastric cancer. Nevertheless, only a small proportion of infected individuals develop gastric cancer and the precise role of *H. pylori* infection in the development of atrophy, intestinal metaplasia and gastric carcinogenesis remains to be elucidated[3]. Recently, it was recognized that certain strains of *H. pylori* were more virulent and characterized by possession of the cytotoxin-associated gene A (*CagA*)[21]. This strain of bacterium is more likely to result in clinically significant disease in Western countries, being more prevalent in patients who develop peptic ulcers as well as gastric cancer [22,23]. However, our previous study demonstrated equally high prevalence of *CagA*-positive strains in patients with gastric cancer, peptic ulcer, non-ulcer dyspepsia, and in control subjects [24]. These results seemed to be consistent with the reports from Japan and China[25,26]. Thus, from current available data, it can be concluded that CagA-positive strains may not contribute an important role in the pathogenesis of gastric cancer.

The current data indicated that the proportion of early, curable gastric cancer was rare among Thai patients. Most of the cases in our study were in the advanced stage (stage III and IV) with a very poor 5-year survival. It is clear that surgical resection of gastric cancer, together with excision of involved lymph nodes, provides the only potentially curative treatment[27]. Even in unresectable cases, palliative resection is still an effective means of providing symptomatic relief. As expected, in our study, the survival rates were significantly higher in patients who had surgical therapy compared to those received only supportive treatment. On the other hand, systemic chemotherapy did not show any advantage in terms of improving the medium survival time. Likewise, the benefits of chemotherapy for advanced disease remain rather limited in most series[28]. Such therapy, therefore, should only be offered to patients at high risk and in carefully controlled clinical trials.

In Japan where the incidence of the cancer is very high, the diagnosis of early gastric cancer (EGC) has progressively increased in the last few years, owing in part to mass screening[29]. Such patients account for 25-60 per cent of operations carried out for gastric cancer and have a good prognosis with a survival rate of over 50 per cent in 5 years after surgery[30]. In Thailand where the incidence of gastric cancer is much lower, the detection of EGC and its effective treatment continues to pose an important problem. Unfortunately, mass screening programs aimed at early diagnosis and treatment of the disease may not be practical in this country because of the unfavorable cost/benefit ratio. Nonetheless, a clinical trial of routine endoscopy for all patients over 40 years of age with minimal upper gastrointestinal symptoms would provide valuable data on the benefits and cost effectiveness of such an approach.

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# สถานะการณ์ของมะเร็งกระเพาะอาหารในคนไทย

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เพื่อต้องการทราบถึงข้อมูลพื้นฐานและการดำเนินโรคของผู้ป่วยมะเร็งกระเพาะอาหารในคนไทย จึงทำการศึกษาย้อนหลังในผู้ป่วยที่มารับการรักษาในโรงพยาบาลจุฬาลงกรณ์ ตั้งแต่ มกราคม 2537 ถึง ธันวาคม 2541 ซึ่งได้รับการวินิจฉัยว่าเป็นมะเร็งกระเพาะอาหารจากผลการตรวจทางชิ้นเนื้อพยาธิวิทยา จำนวนทั้งสิ้น 119 ราย ผลการศึกษาพบว่าเป็นผู้ป่วยชาย 72 ราย (60.5%) หญิง 47 ราย (39.5%) อายุเฉลี่ย 60.16 ± 15.14 ปี อายุที่น้อยที่สุดคือ 22 ปี และมากที่สุดคือ 91 ปี มีผู้ป่วยอายุน้อยกว่า 40 ปี จำนวน 16.8% ระยะเวลาที่ผู้ป่วยมีอาการจนมาพบแพทย์เฉลี่ย 20 สัปดาห์ โดยอาการที่เป็นปัญหาที่นำมามากที่สุดคือ การรู้สึกไม่สบายในท้อง และการมีน้ำหนักลด ผอมลง บริเวณส่วนของมะเร็งที่พบมากที่สุดคือ บริเวณกระเพาะอาหารส่วนปลาย 40.3%, ส่วนกลาง 31.9% และกระเพาะอาหารส่วนบน 15.1% ผลการตรวจชิ้นเนื้อทางพยาธิวิทยาพบว่าเกือบทั้งหมดเป็นชนิด Adenocarcinoma 91.6% และที่เหลือเป็นชนิด Lymphoma 3.4%, Leiomyosarcoma 3.4% ตรวจพบการติดเชื้อ *H. pylori* 68% ผู้ป่วยที่มาพบว่าอยู่ในระยะที่ 2 จำนวน 7 ราย, ระยะที่ 3 จำนวน 11 ราย, ระยะที่ 4 จำนวน 82 ราย ตามลำดับ โดยผู้ป่วยส่วนใหญ่ 89.7% มีการกระจายของมะเร็งไปแล้ว โดยบริเวณที่พบการกระจายของมะเร็งมากที่สุดคือ ต่อมน้ำเหลือง นอกจากนี้อวัยวะที่มะเร็งชอบลุกลามไปอีกคือตับและเยื่อบุช่องท้อง ผู้ป่วยได้รับการรักษาโดยวิธีผ่าตัดบริเวณที่มีมะเร็งออกไปจำนวน 58.9% และไม่สามารถเอาก้อนมะเร็งออกได้จึงทำผ่าตัดโดยวิธี bypass surgery จำนวน 11.1% อัตราการรอดชีวิตในผู้ที่สามารถผ่าตัดได้ สูงกว่าผู้ที่ไม่สามารถผ่าตัดได้ คือ 1.00±0.53 ปีเทียบกับ 0.11±0.03 ปี (p=0.0025). มีผู้ป่วยที่ได้รับการให้ยาเคมีบำบัดร่วมด้วย 35.3% ผลของการตอบสนองต่อการให้ยาเคมีบำบัดพบว่าอัตราการรอดชีวิตไม่แตกต่างกันระหว่างผู้ที่ได้รับและผู้ที่ไม่ได้รับยา สรุปว่ามะเร็งกระเพาะอาหารยังเป็นโรคที่มีความสำคัญต่อปัญหาสาธารณสุข ผู้ป่วยที่มาพบแพทย์ส่วนใหญ่โรคมักจะลุกลามแล้วทำให้การพยากรณ์โรคไม่ดี

**คำสำคัญ** : มะเร็งกระเพาะอาหาร, ผู้ป่วยไทย

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