Early Gastric Cancer: The First Case Series in Thailand

Asada Methasate MD, PhD*,
Atthaphorn Trakarnsanga MD*, Thawatchai Akaraviputh MD*,
Vitoon Chinsawangwathanakol MD, PhD*, Darin Lohsiriwat MD*

** Minimally Invasive Surgery Center, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *Early gastric cancer (EGC) defined as gastric cancer involving up to submucosal layer, regardless of lymph node metastasis, is increasingly found at Siriraj Hospital. Understanding the characteristic of EGC and result of surgical management for EGC can help to choose the optimal treatment. In the present study, the authors reported the first case series in Thailand.*

Material and Method: *The authors analyzed 21 consecutive EGC patients treated with gastrectomy with lymph node dissection between September 2001 and December 2009 at Minimally Invasive Surgery Center, Division of General Surgery, Department of Surgery, Siriraj Hospital, Mahidol University, Thailand.*

Results: *Ratio of EGC to total cases of gastric cancer was increasing yearly, from 1.8% in 2006 to 8.1% in 2009 at Siriraj Hospital. The most common type of EGC was type IIc (66.7%) while type III was found in 19%, and type I in 14.3%. The tumor invaded mucosal layer in 42.9% and submucosal layer in 57.1% of the patients. For N staging, 76.2% of the patients were N0 while N1 was 19% and N2 was 4.8%. Overall, lymph node metastasis was found in 23.8%. For mucosal cancer (m), no lymph node metastasis was seen while for submucosal cancer (sm) five cases (41.7%) had lymph node metastasis, especially in one patient that the metastasis was in N2 group. Lymphatic invasion was seen in 14.3% of cases. All cases with lymphatic invasion were all submucosal cancer. Overall staging was stage 1a in 76.2%, stage 1b in 19%, and stage 2 in 4.8%. Morbidity was seen in 14.3% of the cases. No mortality was seen. The survival was excellent with no recurrence found during the follow-up period of the present study (mean 30.53 months).*

Conclusion: *Surgery for EGC has good results with minimal complications and excellent 5-year survival. Less invasive treatment has become the option for EGC. Understanding the characteristic of EGC and careful selection to assign appropriate treatment is important to improve the result in the treatment of EGC.*

Keywords: *Early gastric cancer, Gastric cancer, Gastrectomy*

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Early gastric cancer (EGC) is defined as gastric cancer involving up to submucosa layer, regardless of lymph node metastasis[1]. It is associated with good prognosis, especially in EGC with no lymph node metastasis in which endoscopic treatment is now standard treatment. However, it is very rare in most of the region outside Japan and Korea where screening and vigorous endoscopic examination results in high prevalence of EGC[2,3]. EGC is associated with excellent 5-year survival with survival rate of over 90% in most reports[4,5].

Correspondence to:
Methasate A, Minimally Invasive Surgery Center, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: 0-2419-8006
E-mail: teams@mahidol.ac.th

In Thailand, it was also thought that this type of lesion rarely exists but due to rapid expansion of esophagogastroduodenoscopy (EGD), the authors now had more experiences with EGC patients. In the present study, the authors reported their experiences of 21 consecutive patients with EGC who were treated at the Department of Surgery, Siriraj Hospital, Mahidol University. The present report focusing on the analysis of the characteristics of EGC and result of surgery for EGC would help us to understand the complexity of this disease, which will become more prevalent in Thailand.

Material and Method

The authors analyzed 21 consecutive EGC patients treated with gastrectomy between September 2001 and December 2009 at Minimally Invasive Surgery

Center, Division of General Surgery, Department of Surgery, Siriraj Hospital, Mahidol University. In all cases, gastrectomy with D2 dissection was performed. Data were prospectively collected in the database for quality control and retrospectively analyzed. All patients were staged according to the staging as proposed by the Japanese Gastric Cancer Association[1]. Preoperative EGD with tissue biopsy and CT scan of the abdomen were done for diagnosis and clinical staging.

During EGD, EGC was thoroughly examined and classified to different type according to Japanese classification[1]. This classification divides EGC into three categories consisting of type I (polypoid type), type II (superficial type), and type III (ulcerative type) (Fig. 1). Moreover, type 2 is further classified into type IIa, IIb, and IIc meaning elevated, flat and depressed type respectively. Numbering of the lymph nodes for grouping and lymph node dissection were done according to the Japanese system. The lymph node dissection for D2 dissection in subtotal gastrectomy included lymph node group 1, 3, 4, 5, 6, 7, 8a, 9, 11p, 12a and 14v. Details of gastrectomy were described in the authors' earlier report[6]. The SPSS 14.0 software package was used for statistical data analysis (SPSS, Chicago, IL, USA). The results were presented in frequency and percent. Mean values were given with their standard deviations.

Results

Twenty-one patients with EGC, consisting of 15 males (71.4%) and six females (28.6%) with the mean age of 62.80 $\pm$ 14.69 years (range 26-87.00 years) participated in this study. Characteristics of the patients are shown in Table 1. The most common presenting symptom was dyspepsia (11 cases, 52.4%) followed by upper GI bleeding (6 cases, 28.60%). Four patients (19%) in the present study had no symptom. Ratio of EGC to total cases of gastric cancer at our department was increasing yearly, from 1.79% in 2006 to 8.11% in 2009 (Table 2). In 2009, EGD was done in 4,441 cases with EGC detected in six cases. Therefore, the detection rate was 0.13% for EGC.

The tumors were located in distal stomach in 61.9% of the cases (13 cases), in the middle part in 23.8% (5 cases) and in the upper part in 14.3% (3 cases). According to endoscopic classification, the most abundant type of EGC in the present study was type IIc (Fig. 2) (66.7%, 14 cases) while type III was found in 19% (4 cases) and type I in 14.3% (3 cases) (Fig. 1). The pathological results showed well-differentiated adenocarcinoma in 52.4% (11 cases) while 19.0% (4 cases) were moderately-differentiated adenocarcinoma and 28.6% (6 cases) were poorly-differentiated adenocarcinoma. Average size of the tumor was 1.93 $\pm$ 1.30 cm.

The tumor invaded mucosal layer in 42.9% (9 cases) and submucosal layer in 57.1% (12 cases). Overall, lymph node metastasis was found in 23.8%. By N staging, 76.2% (16 cases) of the patients were N0 while N1 was 19% (4 cases), and N2 was 4.8% (1 case). No case had distant metastasis. Lymphatic invasion was seen in three cases (14.3%). All cases with lymphatic invasion were all submucosal cancer. Overall staging was stage 1a in 76.2% (16 cases), stage 1b in

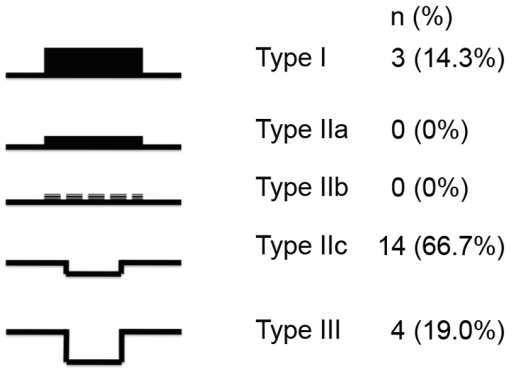

Fig. 1 Classification of EGC (early gastric cancer) according to morphology and distribution of cases in the present series

Fig. 2 The resected specimen of type IIc EGC, showing depressed area at the lesser curvature, lower body of the stomach. Irregular depression and fold convergence is typical for this type of EGC

Table 1. Characteristics of patients with EGC

No.	Symptoms	Sex	Age	Operation	Location	Type	Histology	Size (cm)	T-stage	N-stage	M-stage	Staging	ly
1	Dyspepsia	F	55	subtotal	U	III	por	4	sm	1	0	1b	neg
2	None	M	52	subtotal	L	III	mod	2.4	sm	1	0	1b	pos
3	Upper GI bleeding	M	75	subtotal	M	I	well	4.5	sm	1	0	1b	pos
4	Dyspepsia	F	63	subtotal	L	IIc	well	3.2	m	0	0	1a	neg
5	Upper GI bleeding	M	69	subtotal	L	III	well	3.2	m	0	0	1a	neg
6	Dyspepsia	M	26	subtotal	L	IIc	mod	1.4	sm	0	0	1a	neg
7	None	M	70	subtotal	L	IIc	mod	3.5	sm	2	0	2	neg
8	Dyspepsia	F	77	proximal	U	IIc	well	2.5	m	0	0	1a	neg
9	Upper GI bleeding	M	69	LADG	L	IIc	mod	2.5	sm	0	0	1a	pos
10	Dyspepsia	M	65	LADG	L	IIc	por	0.5	m	0	0	1a	neg
11	Dyspepsia	M	76	LADG	L	III	well	0.5	m	0	0	1a	neg
12	Dyspepsia	M	43	subtotal	L	IIc	well	0.5	m	0	0	1a	neg
13	Dyspepsia	F	68	LADG	L	IIc	well	0.5	m	0	0	1a	neg
14	Upper GI bleeding	M	72	subtotal	L	IIc	well	1.7	sm	0	0	1a	neg
15	None	F	64	subtotal	M	IIc	por	2.5	m	0	0	1a	neg
16	Dyspepsia	M	62	subtotal	M	I	well	1.4	sm	0	0	1a	neg
17	Dyspepsia	F	37	subtotal	L	IIc	por	multiple	sm	0	0	1a	neg
18	Dyspepsia	M	53	subtotal	L	IIc	well	1.3	sm	0	0	1a	neg
19	Upper GI bleeding	M	67	LATG	U	I	well	1	m	0	0	1a	neg
20	Upper GI bleeding	M	87	subtotal	M	IIc	por	2.5	sm	1	0	1b	neg
21	None	M	69	subtotal	M	IIc	por	1.2	sm	0	0	1a	neg

Operation: subtotal gastrectomy (subtotal), proximal gastrectomy (proximal), laparoscopic-assisted distal gastrectomy (LADG), laparoscopic-assisted total gastrectomy (LATG), Location: upper part stomach (U), middle part stomach (M), lower part stomach (L), Histology: well differentiated adenocarcinoma (well), moderately differentiated adenocarcinoma (mod), poorly differentiated adenocarcinoma (por), T-stage: mucosal cancer (m), submucosal cancer (sm), ly: angiolymphatic invasion, N-stage

Table 2. Number of cases of EGC compared to total cases of gastric cancer and esophagogastroduodenoscopy (EGD) cases during 2006-2009

	2006	2007	2008	2009
EGC (cases)	1	1	7	6
Total gastric cancer (cases)	56	48	70	74
Ratio of EGC to total gastric cancer cases (%)	1.79	2.08	10.00	8.11
EGD (cases)	4,526	4,769	4,667	4,441

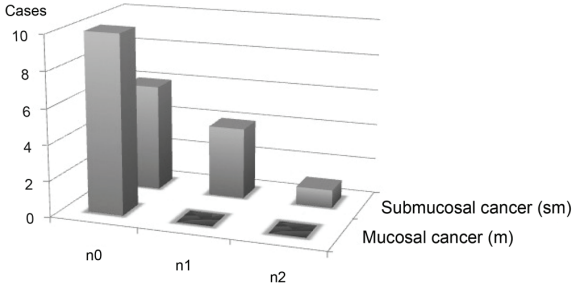

Fig. 3 Incidence of lymph node metastasis comparing mucosal cancer and submucosal cancer

19% (4 cases) and stage 2 in 4.8% (1 case). By peritoneal wash, cytology was positive in one patient.

Relationship between depth of invasion and lymph node metastasis is shown in Fig. 3. For mucosal cancer (m), no lymph node metastasis was seen while for submucosal cancer (sm) 6 cases had no lymph node metastasis but five cases (41.67%) had lymph node metastasis, especially in one patient whom the metastasis was into N2 group.

Regarding type of surgery performed, subtotal gastrectomy was done in 15 cases (71.4%) while laparoscopic-assisted distal gastrectomy (LADG) in four cases (19%), laparoscopic-assisted total gastrectomy (LATG) in one case (4.8%) and proximal gastrectomy in one case (4.8%) (Table 1). The average length of stay was 12.36 $\pm$ 7.23 days. Mean operating time was 209.29 $\pm$ 70.43 minutes and mean blood loss was 355 $\pm$ 190.05 ml. Mean lymph node retrieval was 22.62 $\pm$ 12.25 nodes.

No mortality was seen. Post-operative complications were seen in three cases (14.3%) with intra-abdominal collection in one case, atelectasis in 1case and wound infection in one case. The survival was excellent without any recurrence found during the follow-up period of the present study (mean follow-up period 30.53 months).

Discussion

Gastric cancer is generally associated with poor survival rate[7]. Radical gastrectomy with D2 dissection is the standard treatment for gastric cancer[8,9], however, even with such aggressive surgery, the 5-year survival was still not satisfactory. Detection of EGC is vital in the improvement of surgical management of gastric cancer because EGC has excellent prognosis[10-12] and now EGC is detected much more frequent by than before in Japan and western countries. In Thailand, EGC is considered a very rare type of gastric cancer. However, it is diagnosed with increasing frequency each year. At our department, in recent years, the proportion of EGC was rising up to 8%.

Most abundant type of EGC in the present study was type IIc, followed by type III (ulcerative type) while type IIa and IIb was not found. This is in sharp contrast to other reports from Japan and Europe[13]. The difference may reflect the ability to detect this type of lesion, since the diagnosis needs more extensive examination of the gastric mucosa along with the use of indigocarmine to enhance the contrast of the mucosa. More effort should be exercised to detect this type of lesion.

Symptoms of EGC in the present study also differ from previous reports on EGC[2]. Upper GI bleeding from ulcerative lesion was the second dominant cause of EGC (28.60%) compared to 11% as reported earlier. This may reflect the advanced nature of the gastric cancer in Thailand. Complete follow-up and repeated biopsy of gastric ulcer is important in this aspect.

Major prognostic factor for EGC had been found to be lymph node metastasis[14,15]. The authors' result regarding lymph node metastasis rate of 23.80% was the same as previous reports[16]. Lymph node metastasis was found only in a tumor with submucosal invasion, especially in one patient who was found to have N2 metastasis. In addition, lymphatic invasion

was seen only in cases with submucosal invasion. According to Japanese guidelines, superficial type of submucosal cancer (sm1 and sm2) can be treated with limited gastrectomy (dissection less than D2 dissection) but in the authors' opinion, it is not always easy to differentiate between superficial and deep submucosal invasion, especially for a country like Thailand where there is not much experience in EGC. Moreover, lymphatic invasion had been shown to correlate with poor prognosis[17]. Therefore, for submucosal cancer, gastrectomy with D2 dissection should remain the treatment of choice.

Surgery for EGC, as reported in the present study, has good result with minimal complication and excellent survival. No recurrence was seen. Regarding mucosal cancer, the authors also found no lymph node metastasis, therefore for this type of cancer, the authors agree with the recommendation to treat mucosal cancer with endoscopic treatment or limited gastrectomy[18], provided that the histology revealed well or moderately differentiated adenocarcinoma which occupied approximately 70% of EGC in our study. The authors found one case with mucosal cancer but the lesion was spreading along the mucosa and producing multiple foci of cancer cells. Identification of the extent of the lesion was difficult and this type of cancer is best managed with gastrectomy.

At Siriraj Hospital in the year 2009, rate of detection of EGC was 0.13% (calculated from EGC cases divided by EGD cases), which was not high, taken into consideration the fact that the patients who received EGD at Siriraj Hospital usually had symptoms. Experience of the endoscopists to recognize EGC and meticulous endoscopic examination can improve the detection rate of EGC.

Screening for early gastric cancer has been proved to improve survival in countries with a high incidence of gastric cancer such as Japan[19]. In Thailand, its role is still not determined because the cost of screening is substantial. However, as can be seen in the present report, the incidence of EGC is increasing. Attempt should be done not to miss cases with EGC receiving endoscopic examination. Recognition, differentiation between mucosal and submucosal cancer and accurate demarcation of the extent of the cancer remain the corner stone in the treatment of EGC. Surgical treatment has excellent results. However, less invasive treatment such as endoscopic submucosal dissection (ESD) and laparoscopy-assisted distal gastrectomy (LADG) has become the option of treatment[20]. Understanding the characteristic of EGC and careful selection to choose among these options is important to improve the result of the treatment of EGC.

Potential conflicts of interest

None.

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ผลการผ่าตัดรักษามะเร็งกระเพาะอาหารขั้นแรกเริ่มในผู้ป่วยไทย:รายงานแรกในประเทศไทย

อัษฎา เมธเศรษฐ, อัฐพร ตระการสง่า, ธวัชชัย อัครวิพุธ, วิทูร ชินสว่างวัฒนกุล, ดรินทร์ โล่ห์สิริวัฒน์

ภูมิหลัง: *มะเร็งกระเพาะอาหารขั้นแรกเริ่มหมายถึงมะเร็งทีมีการลุกลามไม่ลึกเกินชั้น submucosal layer โดยไม่คำนึงว่ามีการกระจายไปต่อมน้ำเหลืองหรือไม่ มะเร็งชนิดนี้ ปัจจุบันตรวจวินิจฉัย พบเป็นอัตราส่วนที่เพิ่มขึ้นในโรงพยาบาลศิริราช การรักษามะเร็งกระเพาะอาหารขั้นแรกเริ่มจะได้ผลดี จำเป็นต้องเข้าใจถึงลักษณะพิเศษรวมถึงผลที่ได้จากการรักษาด้วยการผ่าตัด*

วัสดุและวิธีการ: *การศึกษานี้ทำการวิเคราะห์ลักษณะทางคลินิกของมะเร็งกระเพาะอาหารขั้นแรกเริ่ม จำนวน 21 คน ซึ่งได้รับการผ่าตัดที่หน่วยศัลยศาสตร์ทั่วไป ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ระหว่างเดือนกันยายน พ.ศ. 2548 ถึง เดือนธันวาคม พ.ศ. 2552*

ผลการศึกษา: *การศึกษานี้พบว่า มะเร็งกระเพาะอาหารขั้นแรกเริ่มพบได้มากขึ้น โดยมีสัดส่วน ต่อมะเร็งกระเพาะอาหารทั้งหมด 1.78% ในปี พ.ศ. 2549 เพิ่มเป็น 8.11% ในปี พ.ศ. 2552 ชนิดที่พบได้มากสุดได้แก่ ประเภท IIc (66.70%) ขณะที่ประเภท III พบได้19.00% และประเภท I พบได้ 14.30% มีการลุกลามถึงชั้น mucosal 42.90% และถึงชั้น submucosal 57.10% พบว่ามีการกระจายไปยังต่อมน้ำเหลือง 23.80% โดย 19.00% มีการกระจายไปยังกลุ่ม N1 และ 4.80% ไปยังกลุ่ม N2 ไม่พบว่ามีการกระจายไปยัง ต่อมน้ำเหลืองในผู้ป่วยที่มะเร็งลุกลามถึงชั้น mucosa ในขณะที่มะเร็งที่ลามถึงชั้น submucosa มีการกระจายไปต่อมน้ำเหลืองได้ถึง 41.67% โดยเฉพาะ มี 1 รายที่กระจายไปกลุ่ม N2 การลุกลามเข้าท่อน้ำเหลืองพบได้ 14.30% และทุกรายพบเป็นมะเร็งที่ลุกลามเข้าชั้น submucosa*

ระยะของมะเร็งที่พบได้มากที่สุดคือ ระยะ 1a (76.20%) รองลงมาได้แก่ ระยะ 1b (19.00%) และระยะ 2 (4.80%) การรักษาด้วยการผ่าตัดพบว่าเกิดภาวะแทรกซ้อนได้ 14.30% ไม่พบอัตราตายในการศึกษานี้ และไม่พบว่ามีการกลับเป็นซ้ำในผู้ป่วยรายใด (ระยะเวลาการติดตามเฉลี่ย 30.53 เดือน)

สรุป: *การผ่าตัดรักษามะเร็งกระเพาะอาหารขั้นแรกเริ่มสามารถทำได้โดยปลอดภัย และผลการรักษาดีมาก ผู้ป่วยส่วนใหญ่หายจากโรค ปัจจุบันมีการรักษาใหม่หลายชนิดที่อาจไม่ต้องอาศัยการผ่าตัด อย่างไรก็ตาม ความเข้าใจถึงลักษณะพิเศษของมะเร็งกระเพาะอาหารขั้นแรกเริ่ม จะช่วยให้เลือกการรักษาได้อย่างถูกต้อง*