

## Clinicopathological Study of Early Gastric carcinoma

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**Abstract:** We re-evaluated whether the similar surgical procedure has to be needed for early gastric cancer (EGC) as for advanced cancer, especially R2 lymph node dissection, using data from 418 cases of gastric cancer registered in our department during 10 years from 1979 to 1989. In 92 cases the depth of invasion was confined to the mucosal layer (m), and in 51 cases the cancer had invaded the submucosal layer (sm). In all cases in which the EGC was less than 1 cm in length, the lesion was confined to the mucosal layer. All cases of m-cancer which were less than 1.5cm in length and all cases of type IIb EGC were free of lymph node metastasis. In m-cancer cases, lymph node metastases were restricted to nodes #1-#6, and did not occur in #7-#16, while in sm-cancer, such metastases were also found in #7 and #8. In contrast, there was no correlation between lymph node metastasis and histological type or patient age. According to these findings, we recommend the following surgical treatment for EGC: R1-resection is generally indicated for m-cancer and R1 + #7 and #8 lymph node dissection for sm-cancer. Furthermore, local resection (endoscopic therapy) or RO-resection with preservation of the regional lymph nodes appears to be sufficient for type IIb EGC, or for intramural EGC less than 1.5cm in length.

**Key words:** early gastric cancer, lymph node metastasis, recurrent case, limited surgery.

### INTRODUCTION

Gastric cancer is the most common malignancy and a leading cause of mortality in Japan at the present time. Early gastric cancer (EGC) is defined by a depth of tumor invasion which is histologically limited to the submucosal layer of the stomach, regardless of the presence of lymph node metastases. Moreover, it is known

that a fair number of such tumors do not have lymph node metastases if invasion is limited to the mucosal or submucosal layer. Thus, EGC may be curable if the primary lesion and regional lymph nodes are adequately eradicated.

In Japan, during the past 20 years, gastrectomy associated with omentectomy and extended lymph node dissection of the secondary group of nodes, known as R2-resection, generally has been accepted as the procedure of choice

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not only in advanced gastric cancer but even in early cases. This preference is on the potential risk for lymph node metastasis to Group 1, 2 and 3 nodes even in EGC, although the incidence of this is extremely low. Therefore, the question of whether the same surgical procedures are required for EGC as for advanced cancer should be re-evaluated.

In addition, elderly patients with gastric cancer who are not able to withstand aggressive surgery are increasing in numbers every year with the greing of society. Therefore, both early diagnosis and less invasive treatment, such as limited surgery or endoscopic therapy, have also become necessary recently. However, little is known yet regarding the efficacy of such limited surgery in EGC.

The purpose of this study was to evaluate the relationship between the clinicopathologic nature and the mode of lymph node metastases or recurrence in EGC.

## PATIENTS AND METHODS

During the 10 years between 1979 and 1989, the registry in our department was notified of 418 cases of gastric carcinoma, of which 371 (88.8%) were treated by resection. Of these cases, 143 (44% of the whole series) were EGC. Ninety-three of the patients were men and 50 were women. Microscopically, all lesions were adenocarcinoma; in 92 cases the depth of invasion was confined to the mucosa (m-cancer), and in 51 cases the muscularis mucosa had been penetrated but the invasion was limited to the submucosal layer (sm-cancer).

The pathologic descriptions and histology of these cases were reviewed and gastric cancer was classified according to the General Rules for Gastric Cancer Study in Surgery and Pathology<sup>1)</sup>. EGCs were classified macroscopically using the criteria of the Japan Gastroenterologi-

Table 1. The numbering of regional or distant lymph nodes in gastric cancer

numbering	location of lymph node
1	right cardiac lymph node
2	left cardiac lymph node
3	lymph node along the lesser curvature
4	lymph node along the greater curvature
5	suprapyloric lymph node
6	infrapyloric lymph node
7	lymph node along the left gastric artery
8	lymph node along the common hepatic artery
9	lymph node around the celiac artery
10	lymph node at the splenic hilus
11	lymph node along the splenic artery
12	lymph node in the hepato-duodenal ligament
13	lymph node at the superior aspect of the pancreas
14	lymph node at the root of the mesentrium
15	lymph node along the middle colic artery
16	lymph node along the abdominal aorta

This table was quoted from the General Rules for the Gastric Cancer Study and Pathology<sup>1)</sup>.

cal Endoscopy Society<sup>2)</sup>. Classifications included the following: type I polypoid or mass-like lesions; type II, superficial, which may be flat, minimally elevated, or minimally depressed; and type III, cancer associated with a true ulcer. In a type III lesion, the ulcer, by definition, is deeper than the muscularis propria, but the cancer is not deeper than the submucosa. Type II was further subdivided into three subtypes: IIa

Table 2. Tumor size of early gastric cancer and lymph node metastases

m-cancer					
Lymph node metastases	Tumor long diameter (mm)				
	0~0.5	0.5~1.0	1.0~1.5	1.5~2.0	2.0~
n0	3	9	13	14	47
n1(+)	0	0	0	1	3
n2(+)	0	0	0	0	1
n3(+)	0	0	0	0	0
n4(+)	0	0	0	0	0
total	3	9	13	15	51

  

sm-cancer					
Lymph node metastases	Tumor long diameter (mm)				
	0~0.5	0.5~1.0	1.0~1.5	1.5~2.0	2.0~
n0	0	0	7	9	25
n1(+)	0	0	1	2	3
n2(+)	0	0	0	1	2
n3(+)	0	0	0	0	0
n4(+)	0	0	0	0	0
total	0	0	8	12	30

m-cancer + sm-cancer: significant correlation between tumor size and incidence of lymph node metastasis by the Chi-square test,  $p < 0.01$

Statistical analysis was not performed for each of m-cancer or sm-cancer individually because of the limited sample size.

(elevated), IIb (flat), and IIc (depressed).

The locations of regional or distant lymph nodes resected during operations for gastric cancer are listed in Table 1.

EGC may occur as multiple synchronous tumors; the world-wide prevalence of this phenomenon is appropriately 9%. In our study of 149 EGC patients, 151 tumors (6 double tumors, and 1 triple tumor) were identified.

Statistical significance was determined using the  $r \times c$  contingency table of the Chi-square test.

## RESULTS

Microscopically verified metastases in the regional lymph nodes occurred in only 5 pa-

tients (5.4%) out of 92 cases of m-cancer in 9 patients (17.6%) out of 52 cases of sm-cancer. Ten metastases were located in the primary lymph nodes (n1) and four in the secondary nodes (n2); there was no metastases in the tertiary nodes. In order to evaluate whether routine radical lymph node dissection, which has been performed widely in Japan, is adequate for the treatment of such EGCs, the following analyses were conducted.

### 1. Relationship between tumor size and microscopic lymph node metastasis

As shown in Table 2, the incidence of lymph node metastasis correlates well with tumor size for EGC (m-cancer + sm-cancer; significant correlation by the Chi-square analysis,  $p < 0.01$ ). Furthermore, all cases in which the

Table 3. Macroscopic types of early gastric cancer and microscopic lymph node metastases

m-cancer						
Lymph node metastasis	Macroscopic Types(main)					advanced type
	I	IIa	IIb	IIc	III	
n0	5	16	7	52	1	5
n1(+)	1	1	0	1	0	1
n2(+)	0	0	0	1	0	0
n3(+)	0	0	0	0	0	0
n4(+)	0	0	0	0	0	0
total	6	17	7	54	1	6

  

sm-cancer						
Lymph node metastasis	Macroscopic Types(main)					advanced type
	I	IIa	IIb	IIc	III	
n0	0	5	4	29	0	5
n1(+)	1	1	0	3	0	1
n2(+)	0	0	0	2	0	1
n3(+)	0	0	0	0	0	0
n4(+)	0	0	0	0	0	0
total	1	6	4	34	0	7

Table 4. Histological types and microscopic lymph node metastases

m-cancer						
Lymph node metastases	Histological types					Sig
	Pap	Tub1	Tub2	Por	Muc	
n0	4	36	16	15	0	15
n1(+)	0	2	0	1	0	0
n2(+)	0	0	0	0	0	1
n3(+)	0	0	0	0	0	0
n4(+)	0	0	0	0	0	0
total	4	38	16	16	0	16

  

sm-cancer						
Lymph node metastases	Histological types					Sig
	Pap	Tub1	Tub2	Por	Muc	
n0	1	10	13	9	0	6
n1(+)	1	1	0	1	1	1
n2(+)	0	0	0	1	0	1
n3(+)	0	0	0	0	0	0
n4(+)	0	0	0	0	0	0
total	2	11	13	11	1	8

Table 5. Age distribution of early gastric cancer and microscopic lymph node metastases

m-cancer							
lymph node metastases	Age distribution						
	~30	30~40	40~50	50~60	60~70	70~80	80~
n0	1	6	10	25	21	21	2
n1	0	0	1	1	2	0	0
n2	0	1	0	0	0	0	0
n3	0	0	0	0	0	0	0
n4	0	0	0	0	0	0	0
total	1	7	11	26	23	21	2

  

sm-cancer							
lymph node metastases	Age distribution						
	~30	30~40	40~50	50~60	60~70	70~80	80~
n0	1	2	8	10	12	8	1
n1	0	2	0	1	2	1	0
n2	0	2	0	1	0	0	0
n3	0	0	0	0	0	0	0
n4	0	0	0	0	0	0	0
total	1	6	8	12	14	9	1

EGC was less than 1cm in length involved m-cancers. No sm-cancers were seen in this category. Additionally, m-cancers less than 1.5cm in length were all free of lymph node metastasis. These results suggested that if we could measure the depth of the EGC correctly before the operation, lymph node dissection would not be necessary in cases of m-cancer with a diameter less than 1.5cm.

## 2. Relationship between macroscopic types of EGC and microscopic lymph node metastasis.

Although the number of cases studied was quite small (m-cancer: 7 cancer; sm-cancer: 4 cases), no lymph node metastasis was observed in type IIb EGC (Table 3). Regional lymph node involvement has been demonstrated in other types of EGC, except for type III, but at a low incidence. Therefore, we can consider the possibility of limited surgery in case of type IIb EGC.

## 3. Relationship between histological and microscopic lymph node metastasis.

There was no correlation between histological type and lymph node metastasis (Table 4), so we cannot select the procedure for lymph node dissection according to histological type only.

## 4. Relationship between age distribution and microscopic lymph node metastasis.

Since there is a report that a decreased incidence of lymph node metastasis was observed in aged EGC patients, age distribution was investigated in relation to lymph node metastasis (Table 5). No correlation was found in our cases.

## 5. Site of microscopic lymph node metastasis in EGC.

This analysis focused on metastases to the regional lymph nodes of the stomach, which were numbered and grouped by the location of

Table 6. Site of microscopic lymph node metastases

Numbering of lymph node	Metastasis (+)	Metastasis (-)	Incidence of metastasis (%)
<b>m-cancer</b>			
1	2	61	3.2
2	0	20	0
3	2	84	2.3
4	1	82	1.2
5	1	45	2.2
6	2	68	2.9
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7	0	62	0
8	0	66	0
9	0	25	0
10	0	9	0
11	0	15	0
12	0	24	0
13	0	10	0
14	0	1	0
15	0	1	0
16	0	5	0
<b>sm-cancer</b>			
1	0	40	0
2	0	13	0
3	2	48	4
4	2	45	4.3
5	2	24	7.7
6	4	35	10.3
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7	1	39	2.5
8	2	42	4.5
9	0	12	0
10	0	10	0
11	0	11	0
12	0	15	0
13	0	7	0
14	0	0	0
15	0	0	0
16	0	1	0

the primary lesion. The Table 6 shows the status of evaluable lymph nodes which were ex-

cised in EGC cases. In m-cancer, lymph node metastases were restricted to nodes #1-#6, and

were not detected in #7-#16, while in sm-cancer, such metastases were also found in #7 and #8. These results suggested that R1+#7, #8 lymph node dissection was sufficient for curative surgery in EGC cases.

#### 6. Recurrent cases of EGC

Of 143 patients with EGC, 11 died; all of the others were alive at the end of the study (Jan. 1992). One patient in this series, who had sm-cancer, died after surgery; in this case, large lymph node metastases had involved the pancreas, and pancreaticoduodenectomy was performed. The cause of death in other cases included recurrence of gastric cancer in 2 patients, another malignancy (malignant lymphoma) in one case, and disease other than cancer in 8.

One patient with recurrent EGC was a 76-year-old man who had undergone distal gastrectomy with R2 lymph node dissection; the examination of the resected specimen showed a type I lesion at the antrum of the stomach. Histologically, this was a well differentiated adenocarcinoma localized to the mucosa (ly0, v0). No lymph node metastasis was found. Cancer recurred in the liver and paraaortic lymph nodes, and this patient died 5 years and 7 months after the operation.

Another such case involved a 54-year old man, who had sm-cancer of type IIa+IIc at the antrum. He also underwent distal gastrectomy with R2 lymph node dissection. Histologically, this was diagnosed as papillotubular adenocarcinoma (ly3, v0), and the patient already had metastases in the infrapyloric lymph node (n1). He died of paraaortic lymph node metastases, with vertebral recurrence 4 years after the primary operation.

The cumulative 5-year survival rate was 94.6% in m-cancer cases, and 82.4% in the sm-cancer group after gastrectomy.

As described above, there were two cases of

fatal recurrence after R2 resection, but none after RO-and R1 resection in patients with EGC.

## DISCUSSION

The optimal management of gastric cancer at present time includes early diagnosis followed by surgical removal. Progress in the diagnosis of EGC has accelerated improvements in the rate of survival of gastric cancer patients in Japan. In fact, EGC in Japan is associated with five-year survival rates of greater than 90 per cent<sup>3-5</sup>). Our survival data were similar to these reports.

On the other hand, there has been a prevalent philosophy that in any surgical case involving malignancy, extreme caution is required to ensure that no remnants of malignancy or lymphatic metastases are present. Thus, total gastrectomy has become popular, lymph node dissection was extended, and there is wide use of combined resection of the cancer and neighboring organs. Although tumor recurrence after gastric resection for EGC has been rare, it is uniformly lethal. This approach is especially important in young persons in whom long survival is expected with many years at risk for a new tumor. Nonetheless, controversy over surgical treatment of EGC persists. This is as follows; radical lymphadectomy should not be undertaken in patients without regional nodal metastasis. Therefore, conservative, surgery for regional lymph nodes may be appropriate for some patients, provided that the depth of EGC can be evaluated at the time of surgery.

We analyzed retrospectively the clinico-pathological data obtained in our department with EGC cases in an attempt to characterize the disease in relation to lymph node metastasis and ascertain the criteria for selecting appropriate operative procedures.

In our series, lymph node metastasis was

noted in 9.8 percent of EGC cases. Thus, lymph node dissection seems indispensable even in EGC. But since lymph node metastasis in EGC, if occurs, is limited to Group 2 (n2) nodes as shown by our data and other works<sup>6-8</sup>, R2 dissection seems sufficient.

Moreover, the size of the tumor is a major concern because the presence of lymphatic metastasis or involvement tends to increase in direct relation to the tumor size. Larger tumors (>1.5cm) typically have deeper gastric wall penetration and are more likely to have lymph node metastases. Our results are in agreement with those of other researchers in this respect<sup>9,10</sup>. This hypothesis about tumor size has also been applied to the indications for endoscopic therapy for EGC<sup>11</sup>.

There was no difference in the incidence of lymph node metastasis between polypoid and depressed types. However, no patient with a flat type of EGC (IIb) had metastasis to regional lymph nodes and none had recurrence. In contrast, two patients with elevated carcinomas (I and IIa+IIc, respectively) eventually died of metastasis.

Therefore, the selection of suitable patients with EGC for limited surgery should be based on the size, depth, and macroscopic classification of the tumor, as well as the age of the patient, and the presence of concomitant disorders or complications.

In our series, the number of recurrent cases was so few that the presence of lymph node metastasis at the time of surgery was of little relevance for the prognosis of recurrence. Only two subjects had fatal recurrent disease; one had lymph node and liver recurrence while the other had lymph node (#16b1) recurrence followed by vertebral metastasis. One patient was stage I (m, n0, ly0, v0), the other stage II (sm, n1, ly3, v0) by histological evaluation of the surgical specimen. In the former case, lymph node dissection was not indicated in our judgment,

because these factors suggested an excellent prognosis. The latter case suggested that lymph node dissection extended to the paraaortic region may be considered for the primary operation. But in general, we hesitate to perform such extended surgery at this stage.

In conclusion, from the data in the present study, we recommend a new surgical approach for EGC cases as follows:

1) In general, R1-resection is indicated for m-cancer and R1+#7 and #8 lymph node resection for sm-cancer.

2) Local resection or RO-resection with preservation of the regional lymph nodes is usually sufficient for type IIb EGC, or for intramural EGC less than 1.5cm in diameter.

3) Additionally, intra-operative assessment of the depth of parietal infiltration of EGC may be difficult, in which case R2 resection appears to be a safer approach, especially in younger patients who are expected to live for a long time, even though this procedure may sometimes be considered excessive.

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〈和文抄録〉

## 早期胃癌の臨床病理学的検討

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本邦では、この20年来早期胃癌に対しても、進行胃癌と同じ第2群リンパ節郭清が原則としておこなわれてきているが、果してそのような侵襲の大きい根治手術が必要であるか否かの検討を行った。1979年から1989年の10年の間に当教室での418例の胃癌を対象とした。早期胃癌は癌の浸潤が粘膜下層までのものと定義されているが、粘膜内に留まる m 胃癌が92例、粘膜下層に留まる sm 胃癌は51例であった。早期胃癌で長径が1cm以下の症例はすべて、m 胃癌であった。また、径が1.5cm以下の m 胃癌は全例にリンパ節転移が見られず、肉眼型が IIb タイプの早期胃癌においても1例もリンパ節転移は認められなかった。m 胃癌では、リンパ節転移は、胃周辺リンパ節（#1から#6のリンパ節）に留まっており、それ以上の遠隔には転移は観察できなかった。

sm 胃癌では、これに加えるに、#7と#8のリンパ節のみに転移が限局しているという結果であった。その他に組織型、患者の年齢等とリンパ節転移との間の関連についても検討したが、一定の傾向は見られなかった。

以上の結果から考察するに、一般的に m 癌には、R1 郭清を行い、sm 癌には R1+#7, #8 リンパ節郭清を行うのが適応として妥当である。さらに、IIb 型の早期胃癌または、長径1.5cm以下の m 癌が確実な症例には、内視鏡的切除や局所切除のみも十分に適応として考えられる。