

## HISTOPATHOLOGICAL STUDY ON THE PROGNOSIS OF pT<sub>2</sub> GASTRIC CANCER

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### ABSTRACT

The prognosis of gastric cancer was investigated in relation to histopathological grading and amount of interstitial connective tissue in 42 patients with gastric cancer pervading the muscularis propria but without invading the serosa (pT<sub>2</sub> gastric cancer). The 5- and 10-year survival rates of patients with this type of gastric cancer were 76.3% and 47.3%, respectively.

On examining the relation between the prognosis and the histopathological grading, the 5-year survival rate was 82.4% in cases with low degree of differentiation and 66.5% in cases with high and medium degrees of differentiation. No significant statistical difference was seen. The prognosis in relation to the amount of interstitial connective tissue a 5-year survival rate of 91.3% in cases with rich interstitia (scirrhous type), 76.5% in those with intermediate type, and 43.3% in cases with medullary type, thus revealing a favorable prognosis in the first type and a poor one in the last type ( $p \div 0.03$ ). The prognosis was extremely poor in cases of medullary type with low degree of differentiation; these cases had a high rate of mortality from recurrence in the liver and a tendency toward early recurrence. In contrast, a favorable prognosis with a high 5-year survival rate was noted in cases with rich interstitia.

Key Words: pT<sub>2</sub> gastric cancer, histopathological grading, amount of interstitial connective tissue, scirrhous type.

### INTRODUCTION

Despite recent improvement in the survival rate for gastric cancer due to early diagnostic detection and to advances in lymphadenectomy techniques and pre- and post-operative management, mortality still remains a serious problem. Early gastric cancer does not provide much help in the analysis of prognostic factors because of its favorable prognosis, and advanced gastric cancer does not allow adequate analysis of prognostic parameters because of the complexity of factors involved such as recurrence in the peritoneum. Gastric cancer pervading the muscularis propria without invading the serosa pT<sub>2</sub> gastric cancer, on the other hand, is well suited for the purpose of evaluating the relationship between prognosis and histopathological changes because such negative factors as those mentioned above can be excluded. We therefore conducted histopathological investigation of pT<sub>2</sub> gastric cancers in an attempt to elucidate the relationship between recurrence and prognosis. The results indicated that submucosal histopathological grading and the amount of interstitial connective tissue were important factors associated with the prognosis.

### MATERIALS AND METHOD

Of 481 gastric cancer patients seen in our department from Jan. 1969 to Feb. 1983, 42 pT<sub>2</sub>

gastric cancer cases (8.6%) were examined. Pathological examination was conducted using hematoxylin-eosin stained specimens. Following the TNM classification exclusively, pT<sub>2</sub> gastric cancers that pervaded only the muscularis propria were used. pT<sub>2</sub> gastric cancers were macroscopically divided into the early-stage-like type and into types I, II, III and IV, according to borrmann's classification<sup>3) 6)</sup>. The clinical stages were defined by the TNM classification.<sup>3)</sup> The histopathological grading was further divided by the TNM classification into high degree (G1), medium degree (G2) and low degree of differentiation (G3).<sup>3)</sup> pT<sub>2</sub> gastric cancers were also classified by the amount of interstitial connective tissue into medullary, intermediate, and scirrhous type (rich interstitia). The survival rate was calculated by the method of Kaplan Meier, and the significance level was analysed by generalized Wilcoxon test.<sup>3)</sup>

## RESULTS

The anatomical site of pT<sub>2</sub> gastric cancer was the lower third of the stomach in 20 patients, the middle third in 18, and the upper third in 4. The macroscopic findings (Table 1), revealed 2 cases of Borrmann type I, 11 of type II, 11 of type III, 0 of type IV, and 16 of early-stage-like type. No correlation was seen between pT<sub>2</sub> gastric cancer types and the amount of interstitia as shown in Table 2. Concerning the clinical state, as shown in Table 3, stage II patients were predominant in both the intermediate and scirrhous types, followed by stage III patients. There was no case of stage I according to the TNM classification.

The survival rate of pT<sub>2</sub> gastric cancer patients after curative resection was 76.3% for 5 years and 47.3% for 10 years. On examining the relation between the histopathological grading and prognosis, the 5-year survival rate was 82.4% in patients with low degree of differentiation (G3) and 66.5% in those with high and medium degrees of differentiation (G1 and G2, respectively), as shown in Fig. 1. No statistical difference in survival was obtained ( $p \doteq 0.3$ ).

On examining the relation between the amount of interstitial connective tissue and the survival rate, as shown in Fig. 2, the 5-year survival rate was 91.3% for scirrhous type, 76.5% for intermediate type, and 43.3% for medullary type. This reflected a favorable prognosis for the scirrhous type and a poor prognosis for the medullary type ( $p \doteq 0.03$ ). Table 4 lists the deaths in 10 cases of recurrence after curative resection. Especially remarkable were the deaths of

Table 1. Macroscopic findings

Type	NO OF Case S
Borrmann I	2
II	11
III	11
IV	0
Early-stage-like	16

patients in cases 4, 5 and 6 of medullary type with low degree of differentiation (G3) by liver metastasis shortly after curative resection.

Table 2. Correlation between types of pT<sub>2</sub> gastric cancers and amount of interstitial connective tissue

Type	amount of interstitial connective tissue		
	S	I	M
B- I	No.	No.	No.2
B- II	3	6	3
B- III	3	7	2
Early-stage-like	9	5	2

B- I Borrmann I type S : scirrhouous type

B- II Borrmann II I : intermediate type

B- III Borrmann III M : medullary type

(Numbers in the table indicate the number of patients)

Table 3. Clinical stage in each group

		G1	G2	G3	GX	Total
Medullary type	Stage I	-	-	-	-	0
	II	-	2	1	-	3
	III	1	1	3	-	5
	IV	-	-	1	-	1
Intermediate type	Stage I	-	-	-	-	0
	II	2	3	5	1	11
	III	1	1	2	-	4
	IV	1	1	-	-	2
Scirrhouous type	Stage I	-	-	-	-	0
	II	-	2	8	-	10
	III	-	-	3	-	3
	IV	-	1	1	-	2

The Numbers in the table indicate the number of patients.

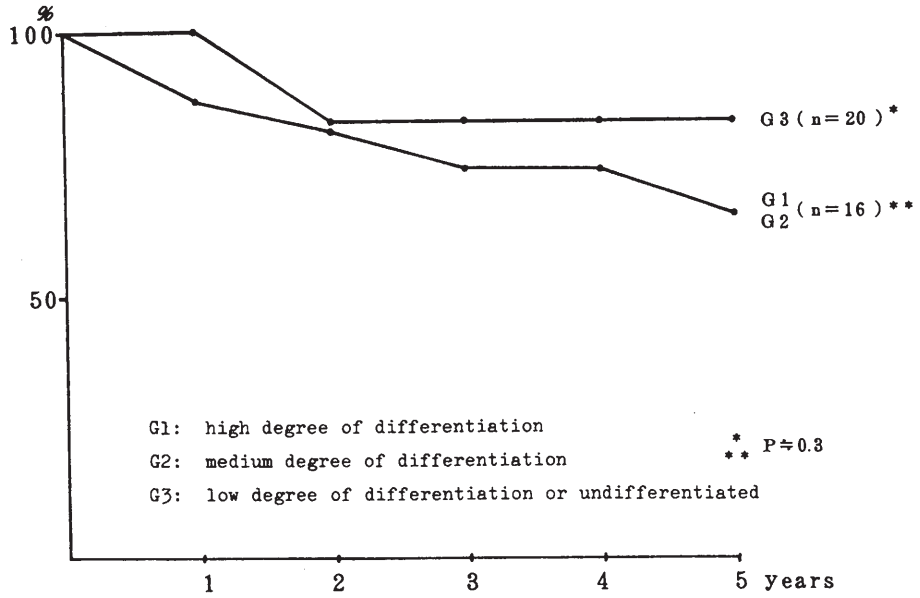


Fig. 1. Survival rate by differential histopathological grading.

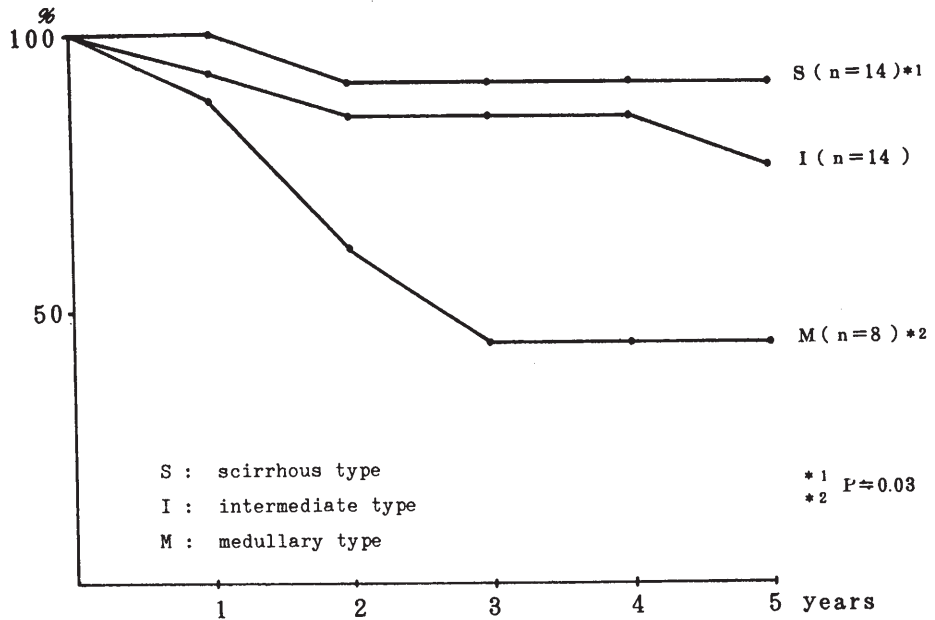


Fig. 2. Survival rate by differential amount of interstitial connective tissue.

Table 4 Differential histopathological grading and amount of interstitial connective tissue of deaths by recurrence

Case	Histopathological grading*	Interstitial connective tissue**	Duration of survival	Site of Recurrence
1	G1	I	6y10m	lung lymph node
2	G2	I	9m	local
3	G2	S	8y	bone
4	G3	M	1y1m	liver
5	G3	M	4m	liver
6	G3	I-M	1y9m	liver
7	G3	S	6y4m	local
8	G3	I	5y6m	local
9	G2	M	2y3m	liver
10	G3	I	1y	lymph node

\*G1: High degree of differentiation

G2: Medium degree of differentiation

G3: Low degree of differentiation or undifferentiated

\*\*S: Scirrhus type

I: Intermediate type

M: Medullary type

## DISCUSSION

pT<sub>2</sub> gastric cancers not only rank between early stage cancers and advanced cancers but also are best suited for evaluation of the therapeutic course because factors involved in peritoneal recurrence can be excluded. Interesting results were obtained in the present clinico-pathological investigation of pT<sub>2</sub> gastric cancer, especially in terms of the relation between the histopathological grading and the amount of interstitial connective tissue. The 5- and 10-year survival rates after curative resection were 76.3% and 47.3%, respectively. The lower 10-year survival rate may be largely due to death from other causes.<sup>2)</sup> In terms of the relation between the histopathological grading and prognosis, the 5-year survival rate for patients with low degree of differentiation (G3) was not lower than that for patients with high (G1) or medium (G2) degrees of differentiation. In advanced gastric cancer, the prognosis of patients with a low degree of differentiation (G3) is somewhat poor, presumably due to peritoneal recurrence.<sup>5)</sup>

In terms of the relation between the amount of interstitial connective tissue and prognosis, the prognosis proved better in the scirrhus type and worse in the medullary type. This finding is reported for the first time in the literature. Thus, although its prognosis has been known to be poor<sup>1)</sup>, the scirrhus type itself may by no means be highly malignant. Kamei<sup>4)</sup> measured the mitotic index of gastric cancer cells and reported that the mitotic index was  $52.8 \pm 13.5$  in the medullary type,  $54.1 \pm 16.9$  in the intermediate type and  $18.4 \pm 8.1$  in the scirrhus type, thus showing a lower index and hence slower proliferation of carcinoma cells in the scirrhus type.<sup>4)</sup>

On examining the relation between the pattern of recurrence and the amount of interstitial connective tissue after curative resection, hepatic metastasis occurred in 3 patients with medullary type and low degree of differentiation (G3). These patients died within only 4 months

to 1–3/4 years after the operation. Hepatic metastasis is usually considered to occur frequently in cases with high degree of differentiation (G1) and in cases of severe venous invasion.<sup>7)</sup> Our data suggest that possibility of hepatic metastasis in patients with low degree of differentiation (G3) seems also high in these with medullary type, though their numbers are few. This suggests the need for effective postoperative chemotherapy if the prognosis should appear unfavorable. In contrast, in terms of the relation between the histopathological grading and the amount of interstitial connective tissue in fair prognostic survivors living for more than 5 years, the scirrhous type with low degree of differentiation (G3) proved to have a favorable prognosis. A considerable difference in prognosis results from the difference in the amount of interstitial connective tissue, despite the same histopathological grading.

These results suggested that the amount of interstitial connective tissue affected the prognosis more than histopathological grading or that G3 type of scirrhous carcinoma was not of low-grade cell differentiation and instead showed a high degree of transformation. In fact, the prognosis of medullary type and G3 carcinoma was poor compared with the medullary type of well-differentiated carcinoma. From the present investigation, which focused mainly on the histopathological aspects of the features of pT<sub>2</sub> gastric cancer, it was concluded that the histopathological grading and the amount of interstitial connective tissue play important roles in the prognosis. Thus, the TNM classification was demonstrated to be as valid as the traditional classification for the prognosis of gastric cancer.

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