

RELATIONSHIP BETWEEN INTERSTITIA AND PROGNOSIS OF GASTRIC CARCINOMA

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ABSTRACT

Excluding cases of early carcinoma, curative surgery for gastric carcinoma was performed in 149 patients from 1969 to 1978. Among them 77 had adenocarcinoma with a large amount of interstitial connective tissue (scirrhous type), and 72 had adenocarcinoma with a comparatively small amount of connective tissue (non-scirrhous type). The overall survival rate was low among those with scirrhous type ($P=0.095$). However, in comparing 14 cases (18.1%) of pT2 carcinoma of scirrhous type with 22 cases (32.7%) of pT2 carcinoma of non-scirrhous type, the survival ratio of those of scirrhous type exceeded that of those of non-scirrhous type ($P=0.045$). The proliferation of interstitia in metastatic lesions of the lymph nodes was not always the same as that in the primary lesion. The prognosis of carcinoma in cases of lymphatic metastasis with a large amount of connective tissue (scirrhous type) was better than that in those with a small amount of connective tissue (non-scirrhous type).

Keywords: Tumor interstitia, Scirrhous gastric carcinoma

INTRODUCTION

An attempt was made to study the relationship between the amount of interstitia and the clinical prognosis of gastric carcinoma. Although scirrhous carcinoma was assumed to show poor prognosis,¹⁻⁶) it was difficult to determine the prognosis of scirrhous cases in comparison with other types of carcinoma. Scirrhous carcinoma, for example, tends to be diagnosed at a far advanced stage and has not been found in patients with early carcinoma. Therefore, prognosis and the amount of interstitial connective tissue were analyzed in cases of pT2, pT3+4, respectively. According to the General Rules for Gastric Cancer Study in Surgery and Pathology, scirrhous carcinoma is classified as carcinoma with a large amount of interstitial connective tissue.⁷⁾ In this study, all cases of gastric carcinoma were divided into two groups according to the amount of interstitia, i.e., scirrhous type and non-scirrhous type.

MATERIALS AND METHODS

Regardless of the type of cells, gastric carcinoma was classified into scirrhous type and non-scirrhous type.⁷⁾ Carcinoma with a large amount of interstitial connective tissue was classified as

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Received for Publication October 1, 1984

scirrhous carcinoma. Non-scirrhous carcinoma included the intermediate and medullary types of carcinoma.⁷⁾

There were 254 patients who underwent curative surgery from 1969 to 1978, but 95 cases of early carcinoma were excluded from these. All of the remaining cases were divided into a scirrhous group (77 cases) and a non-scirrhous group (72 cases). Cases of pT2 carcinoma (36 cases), which showed tumor invasion to the muscularis propria without invasion to the serosa, were also divided into a scirrhous group (14 cases) and a non-scirrhous group (22 cases).⁸⁾

Lymph node metastasis was classified into 3 groups as follows: 1) minor metastasis localized in the periphery of lymph nodes or growing in the lymphatic vessels without invasion of vessel walls, 2) metastasis showing rich interstitia, and 3) metastasis with a lesser amount of interstitia.

The survival rate of patients in the various groups was observed for up to 5 years, and a statistical evaluation of the survival rate was made according to Kaplan Meier's method⁹⁾ and Mantel-Haenszel method.¹⁰⁾

RESULTS

Table 1 indicates the number of patients according to the classification of depth of invasion (pT1, pT2, pT3+4) and amount of interstitia (scirrhous type, non-scirrhous type). All cases underwent curative surgery.

Table 1. Number of cases classified by depth of invasion and amount of interstitia

Depth of invasion	Scirrhous type	Non-scirrhous type
pT1	6	89
pT2	14	22
pT3+pT4	63	50

(Cases of pT1 were excluded in Fig. 1, Fig. 2 and Fig. 3)

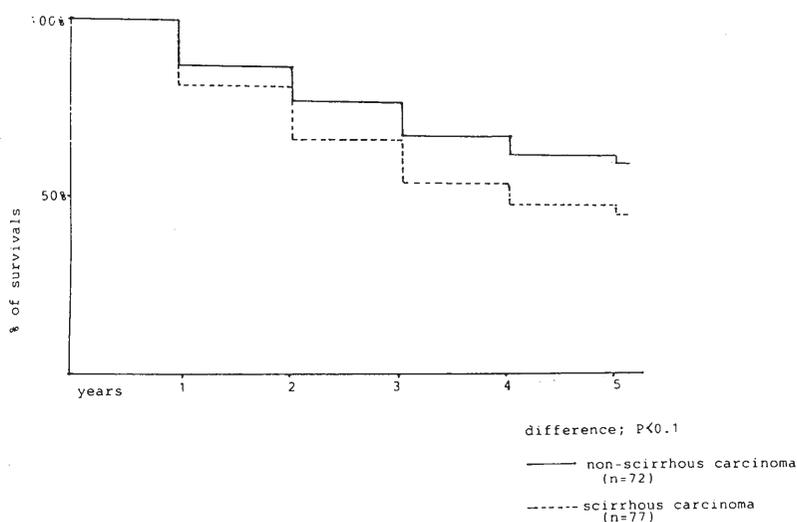


Fig. 1 Survivals of gastric carcinoma cases after curative surgery

Fig. 1 shows the comparative survival time of 72 non-scirrhou and 77 scirrhou carcinoma patients. The percent of survival for those with non-scirrhou carcinoma exceeded that for patients with scirrhou carcinoma, although not to a statistically significant degree ($P=0.095$). The group of pT1 cases was excluded from the comparison because scirrhou-type cases were extremely few (Table 1).

Fig. 2 shows the survival rates in 36 cases of pT2. The rate of the scirrhou type ($n=14$) exceeded that of the non-scirrhou type to a statistically significant degree ($P < 0.05$).

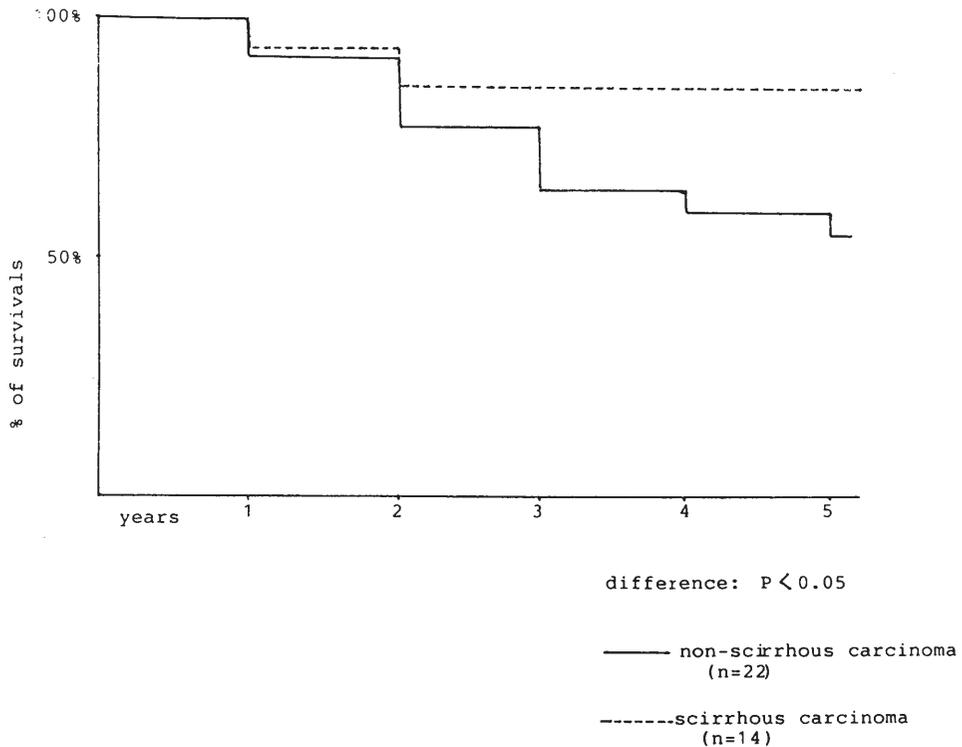


Fig. 2 Survivals of pT2 carcinoma cases after surgery

The amount of interstitia was not always the same in the primary and metastatic lesions. Table 2 indicates the number of patients classified by the amount of interstitia in the primary and lymph node metastatic lesions. Percent of lymphatic metastasis in the scirrhou type was overwhelmingly higher than that in non-scirrhou type in the pT3+4 group, but was not significantly different in the pT2 group.

As shown in Fig. 3, the survival rate of type 1 group (minor metastasis to lymph nodes) was significantly greater than that of the other 2 groups. The survival rate of type 2 group (lymphatic metastasis with rich interstitia: $n=26$) was greater than that of type 3 group (lymphatic metastasis with less interstitia: $n=28$), though there was no statistical significance ($P=0.11$).

Table 2. Number of cases classified by amount of interstitia in primary and lymph node metastatic lesions

Depth of invasion	*Scirrhou type			*Non-scirrhou type		
	**Type 1	Type 2	Type 3	**Type 1	Type 2	Type 3
pT1	(6)	0	1	0	0	1
pT2	(14)	1	0	3	1	2
pT3+pT4	(63)	9	18	14	3	7

* primary lesion

** metastasis in lymph nodes

type 1: minor metastasis

type 2: metastasis with rich interstitia

type 3: metastasis with less interstitia

() Number of patients with & without metastasis

(pT1 case was excluded in Fig. 3)

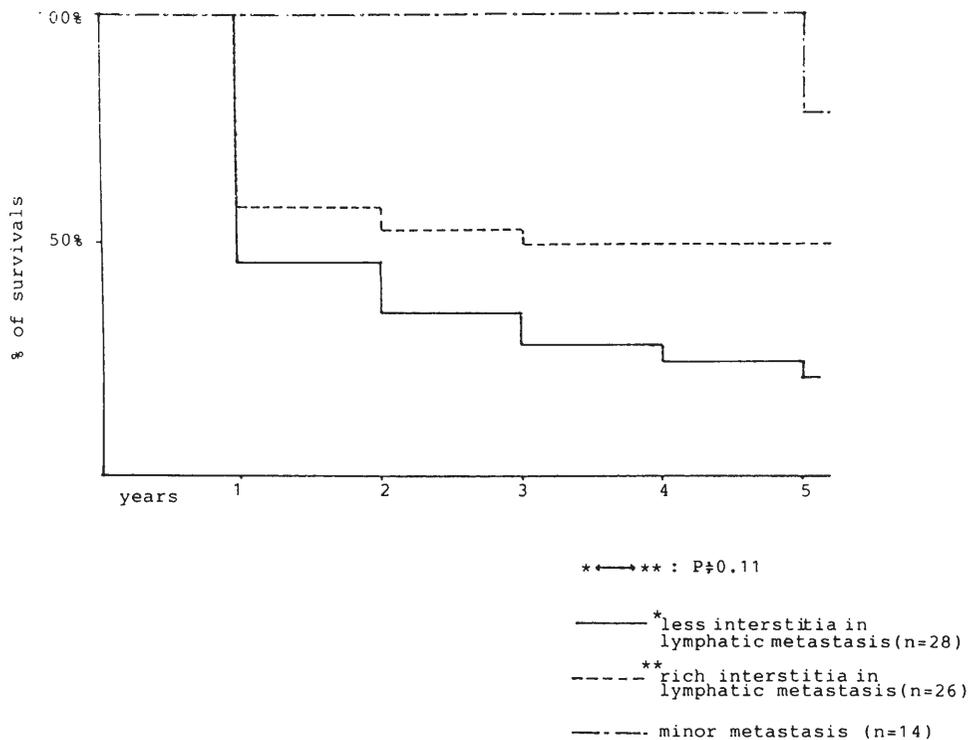


Fig. 3 Survivals of carcinoma cases with lymphatic metastasis after curative operation

As shown in Table 3, the poorly differentiated type was more frequently observed in the scirrhou type than in the non-scirrhou type ($p < 0.002$). No well-differentiated type was observed in the scirrhou type. Poorly differentiated carcinoma and scirrhou carcinoma were frequently observed in females. The survival ratio for those with a poorly differentiated carcinoma was less

than that for those patients with a more highly differentiated carcinoma, i.e., the survival rate at the 5th post-operative year was 40.8% in the former group and 60.9% in the latter group ($p=0.08$). In those with pT2 carcinoma, as shown in Table 4, the number with poorly differentiated carcinoma was the same as the number with more highly differentiated carcinoma, and the survival rate was not significantly different between these groups.

Table 3. Number of gastric carcinoma cases which underwent curative surgery classified by sex, cell type, and amount of interstitia

Interstitia	Sex	Poorly differentiated type	Moderately or well-differentiated *type	Total
Scirrhou type	male	21	29	50
	female	15	12	27
Non-scirrhou type	male	11	49	60
	female	5	7	12
Total		52	97	149

*No case of well-differentiated type was observed among cases of scirrhou type.

Table 4. Number of pT2 gastric carcinoma cases classified by sex, cell type, and amount of interstitia

Interstitia	Sex	Poorly differentiated type	Moderately or well-differentiated type	Total
Scirrhou type	male	5	7	12
	female	2	0	2
Non-scirrhou type	male	7	8	15
	female	4	3	7
Total		18	18	36

DISCUSSION

Prognosis of gastric carcinoma is influenced by lymphatic metastasis, cell type, peritoneal spread (P factor), infiltration of immune competent cells and other factors. Carcinoma cells invading the serosa (pT3, pT4 pTx) in the scirrhou type tend to spread widely in the stomach wall and to induce peritoneal metastasis. The pT2 carcinoma was selected for the comparison of prognosis because pT2 carcinoma may not cause direct peritoneal spread, thus avoiding the influence of P factor.⁸⁾ Here it was revealed that prognosis was significantly better in those with scirrhou type. We previously reported that the connective tissue surrounding the tumor cells inhibited the proliferation of tumor cells in animal experiments¹¹⁾ and that the mitotic ratio of human gastric carcinoma was significantly low in cases of scirrhou type.¹²⁾ These results are meaningful in considering the influence of interstitial connective tissue, although scirrhou carcinoma, as it is termed in this study, may include various types. Our study indicated that those with a poorly differentiated carcinoma had a poor prognosis. Well-differentiated carcinoma was not found in the scirrhou type, and the frequency of the poorly differentiated type in the scirrhou carcinoma exceeded that of the non-scirrhou type.⁷⁾ Nevertheless, those with scirrhou carcinoma did not have a poor prognosis among the pT2 group, and those with lymph node metastasis with rich interstitia had a good prognosis as compared to those with less interstitia. These results suggest

that interstitial connective tissue serves as a protection against invasion by malignant cells.

The genesis of scirrhous carcinoma, as a narrow term, is unknown,^{1,5,6)} although it is thought that this type of carcinoma may develop from an early gastric carcinoma which forms a superficial ulcer.⁴⁾ It is also unknown whether the narrow term scirrhous carcinoma may need to be redefined somehow in the future.

ACKNOWLEDGEMENT

This study was supported by grants from the Ministry of Health and Welfare, Japan, and by the Imanaga Foundation.

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