Table

Patient characteristics

Characteristic		No. of patients
Patients		32
Male/Female		21/11
Age yrs, median (range)	63 (38–75)	
Performance status (Karnofsky), median (range)	70% (60–90)	
Cell type		
Adenocarcinoma		22
Epidermoid carcinoma		8
Large cell anaplastic carcinoma		2
Extent of disease		
Stage III, M0		5
Stage III, M1		27
Evaluable for response		26
Previous treatment		
None		16
Prior chemotherapy		8
Prior radiotherapy		2
Prior interferon		2
Prior surgery		4

leukopenia (nadir 0.5 × 10^9/l) 8 days after her first cycle of 185 mg of epirubicin died at the 9th day of bilateral pneumonia. One patient refused further treatment after 2 cycles due to increased attacks of pain of angina and she died 4 months after discontinuation of epirubicin from acute myocardial infarction (verified at autopsy). No other cardiac toxicity was noted. Two patients had mild mucositis (grade 2), one had diarrhea (grade 2), one had fever (grade 2) and one headache (grade 2). Nausea and vomiting were mild in one patient (grade 2) and severe in 5 (grade 3).

Despite the observation of 2 PRs, the median survival time was only 5 months and the 1-year survival was 20%. No patient survived for 2 years. Fifty percent of the patients, however, were previously treated and 84% of them had extensive disease. Toxicity in our study was moderate compared with that in other recent studies on chemotherapy for NSCLC; 48% of treated patients had grade 3–4 toxicity. We conclude that the benefit of 4-epirubicin for patients with advanced NSCLC was minimal under the conditions of our study.

Key words: Lung cancer, non-small cell, epirubicin.

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ESTROGEN RECEPTORS IN GASTRIC CANCER

The presence of steroid receptors has been well-documented in hormonal-dependent cancers, such as breast cancer, prostate cancer and endometrial cancer (1–3). However, recently it has been reported that tumors believed to be non-target organs for sex steroid hormones also have detectable amounts of estrogen and progesterone receptors (ER and PgR). For example, ER positive tumors from the gastrointestinal tract have been reported on (4–7). The aim of the present study was to correlate possible presence of ER and PgR in gastric carcinoma to other prognostic features such as morphologic mode of growth and grade of differentiation.

Material and Methods. Resected stomach tissue from 21 consecutive patients with primary gastric cancer was used. Specimens of the gastric cancer were obtained immediately after gastric resection and stored at −80°C until the time of assay. The methods of assay was previously described by Fernö et al. (8, 9). ER and PgR were measured in the cytosol with enzyme immunoassay according to kit instructions (Abbott Laboratories, North Chicago, Illinois, USA). The level of sensitivity for the assays was 1.0 fmol/ml and the receptor concentrations were expressed as fmol/mg protein, which was determined according to Lowry et al (10).

Table

Characteristics and receptor values of the patients

Case No.	Sex	Age	Borrman type	Histological differentiation	Er PgR (fmol/mg protein)
1	F	76	B 2	poor	1.7 0
2	M	72	B 4	poor	3.2 0
3	F	74	B 2	poor	1.0 0
4	F	79	B 2	poor	1.9 0
5	M	63	B 2	moderate	1.7 0
6	M	74	B 1	poor	1.7 0
7	F	66	B 2	poor	1.3 0
8	M	79	B 2	poor	0.8 0
9	F	81	B 2	poor	9.4 0
10	M	82	B 2	poor	0.9 0
11	F	62	B 4	poor	6.4 6.2
12	F	68	B 2	moderate	0 0
13	M	69	B 1	moderate	1.6 0
14	M	62	B 3	poor	0.4 0
15	M	66	B 3	moderate	0 0
16	M	62	B 2	moderate	0 0
17	M	71	B 3	poor	1.6 0
18	F	76	B 3	moderate	0.9 0
19	M	83	B 3	poor	2.2 0
20	M	83	B 2	moderate	0.8 0
21	M	67	B 3	poor	0 0

The tumors were histologically classified as well, moderately, or poorly differentiated (none of the cancers were actually well differentiated) and morphologically classified according to Borrman's classification of gastric cancer (11). Type 1 is a well-demarcated polypoid lesion that protrudes into the lumen of the stomach without ulceration. Type 2 is an ulcerated lesion surrounded by a circumscribed, elevated border. Type 3 is an ulcerated lesion surrounded by an uncircumscribed border. Type 4 is characterized by diffuse infiltration of cancer cells that have a strong stromal reaction and show a scirrhotic growth pattern, where the cancerous area is not well-limited. Statistical analyses were made using the Mann-Whitney U-test.

Results. Thirteen males and 8 females were included. Two of the tumors had a growth pattern classified as Borrman type 1, 11 as type 2, 6 as type 3, and 2 as type 4. Ten of the cancers were poorly differentiated, 4 were moderately-poorly differentiated and 7 were moderately differentiated. There was no correlation between grade of classification and classification according to Borrman, nor between sex or age and grade of differentiation (Table 1).

The range of ER concentration in our study was 0 – 9.4 fmol per mg protein, with a mean value of 1.8 and median value of 1.3. Four tumors did not contain detectable amounts of ER receptors, and only 2 tumors had ER concentrations above 5 fmol ER/mg protein. Only 1 patient presented with PgR receptors in a concentration of 6.2 fmol PgR/mg protein. This patient was one of the two with the highest levels of ER receptors. There was a statistically significant lower ER receptor concentration in moderately differentiated tumors compared with poorly differentiated ($p = 0.042$). The four tumors with the highest ER values were all poorly differentiated cancers. On the other hand three of the four patients without any detectable amounts of ER had moderately differentiated cancers. We could not find any correlation between ER concentrations and Boorman's classification of the tumors.

Discussion. Since the presence of ER and PgR in gastric cancer was first reported by Tokunaga et al. (6), there has been a discussion whether or not ER and PgR are correlated with histological differentiation in patients with gastric cancer. The Tokunaga group reported 2 ER positive cases (out of 10 cases), both histologically characterized as undifferentiated cancers. Sica et al. (5) reported on 8 ER positive cases and 14 PgR positive cases among 56 patients with gastric cancer. The gross and microscopic characteristics of these positive cases, however, were, not described in the reports. Later Tokunaga et al. (7) reported 17 ER positive gastric tumors (out of 86 cases) which were grossly characterized as Borrman type 4 and microscopically as diffuse type with scirrhous growth pattern. In these studies, dextran-coated charcoal or sucrose density gradient centrifugation methods were used for receptor detection.

Immunohistological methods using monoclonal antibodies to human ER have lately been used to detect ER in gastric cancer. Yokozaki et al. (12) reported 28 ER positive cases among 71 poorly differentiated cancers and 2 ER positive specimens among 37 well-differentiated cancers. Harrison et al. (13) reported that 56% of 95 specimens with human gastric cancer were ER positive, with a slightly lower proportion of ER positive tumors in the poorly differentiated group compared with the moderately differentiated group.

In our study we have used an enzyme immunoassay method for ER and PgR detection. This method is the same one as we routinely use for breast tumors. However, the concentrations of ER and PgR in breast cancers are often higher than those we have found in gastric cancer. After the present study was made, the immunohistochemical method for detecting ER appeared and it seems likely that this method could detect scattered ER positive cells which may not produce a positive biochemical assay (13). Thus, different assay methods might, at least partially, explain the differences in ER concentrations in our study compared to others.

The histological type of ER positive gastric carcinomas has predominantly been described as poorly differentiated and more seldom as well-differentiated. Our report seems to confirm this observation. Tokunaga et al. (7) previously reported that all ER positive gastric cancers were characterized as Borrman type 4, which gave considerable hope for ER-measurements as a prognostic factor. Unfortunately, no such discriminating prognostic ability of the receptor status could be confirmed in the present study or in several other studies.

From recent Japanese studies (14–16) on tamoxifen and chemotherapy in gastric cancer, a survival advantage has been reported for tamoxifen-treated patients. The results of these studies, however, do not agree with the results in the larger study reported by Harrison et al. (13), which showed no beneficial effect of tamoxified on survival.

In summary, we found low levels of ER in specimens of gastric cancer but there was no correlation with morphological or histological features. Our findings at present give not incitament for hormonal or antihormonal treatment of gastric cancer patients.

Key words: Gastric cancer, estrogen receptors.

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