Abstract. Background: We evaluated the results of chemosensitivity testing for gastric cancer using a 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay in terms of the correlation of chemosensitivity and clinicopathological findings. Patients and Methods: We analyzed 435 consecutive patients with gastric cancer treated between January 1991 and January 2002. Highly purified fresh human gastric cancer cells were obtained from 485 lesions including 415 primary tumors and 70 metastatic tumors. Results: CDDP and 5-FU were more potent drugs than MMC, ADR and VP-16. The chemosensitivity of metastatic tumors was lower than that in primary tumors. The chemosensitivity in differentiated cancer was equivalent to that in undifferentiated cancer. The manner of tumor invasion and clinical stage affected chemosensitivity for some drugs. Conclusion: Our results suggest that individual chemosensitivity testing is essential to individualize chemotherapy for gastric cancer.

Chemotherapy plays an important role in the treatment of patients with advanced gastric cancer although radical surgery is the only curative treatment. The majority of patients with advanced gastric cancer require treatment with anti-cancer agents at some point in the course of their disease. Chemotherapeutic regimens for cancer patients are usually based on the statistical results of clinical trials (1, 2) or are defined by the histological type of tumor rather than the sensitivity of the tumor cells to each anti-cancer drug (3). Many regimens have been applied in clinical trials and the clinical outcomes evaluated (4, 5). Randomized trials comparing chemotherapies with best supportive care provide consistent evidence that cytotoxic treatment is of some benefit (6-8). Nevertheless, there have been no major improvements in the overall prognosis of advanced gastric cancer. In advanced gastric cancer, response rates (RRs) of 20%-30% have been reported with single agents such as 5-FU, MMC, ADM and CDDP. With a combination, RRs may be as high as 30-50%. However, the duration of response with these regimens tends to be short, and complete responses are rare. In addition, some regimens are relatively toxic, rendering them inappropriate for many patients. To date, no particular regimen has been shown to be superior to others in terms of the prolongation of overall prognosis. In order to develop the clinical efficacy of chemotherapy for gastric cancer and to avoid adverse effects, it is important to assess individual sensitivities to anti-cancer drugs. A diagnostic assay that is capable of predicting the response to a given anti-cancer agent could help to improve the clinical outcome of gastric cancer patients. It is desirable that individualized chemotherapy should be performed according to the chemosensitivity of tumor cells in each patient. So far, various types of chemosensitivity tests for cancer patients have been developed and the clinical usefulness reported (9-11). We also previously reported the clinical usefulness of chemosensitivity testing using an MTT assay for patients with gastric cancer, colon cancer and esophageal cancer (12-14). The MTT assay is a rapid and quantitative colorimetric system for determination of the chemosensitivity of tumor cells (15). We were able to eliminate the contamination of non-malignant cells by performing two steps of discontinuous gradient centrifugations to obtain highly purified tumor cells. In order to establish reliable chemosensitivity testing as a routine examination in chemotherapy, it is essential to verify the results of
chemosensitivity in a large number of patients. In the present study, we evaluated the results of chemosensitivity testing with highly purified tumor cells using an MTT assay in 435 cases of gastric cancer in terms of the correlation with clinicopathological findings and chemosensitivity. This is the first attempt to analyze large numbers of results of chemosensitivity in patients with gastric cancer.

**Patients and Methods**

**Patients.** A total of 435 consecutive patients with gastric cancer were analyzed in this study. All patients were registered at the Wakayama Medical University Hospital, Japan, in the period from January 1991 to January 2002. The mean age was 60.4±11.0 years. The ratio of males to females was approximately 5:2. The clinical stage of the patients was determined according to the TNM classification. Tumor specimens and ascites were obtained for diagnosis or therapeutic indications and the informed consent of patients was obtained for the use of samples for chemosensitivity tests in accordance with the guidelines of the Ethical Committee on Human Research, Wakayama Medical University. Surgical specimens were obtained from 415 primary tumors, 25 metastatic lymph nodes, 4 metastatic liver tumors and 4 metastatic ovarian tumors. Malignant ascites were collected for analysis from 37 patients with disseminated gastric cancer.

**Drugs.** The anticancer drugs tested were cisplatin (CDDP), etoposide (VP-16) (Nippon Kayaku Co., Tokyo, Japan), mitomycin (MMC), doxorubicin (ADR), 5-fluorouracil (5-FU) (Kyowa Hakko Kogyo Co., Tokyo, Japan), SN-38 (active metabolite of irinotecan) (CPT-11) (Yakult Co., Tokyo, Japan) and docetaxel (DOC) (Aventispharma Co., Tokyo, Japan). Each drug was diluted in a complete medium at 10-fold therapeutic peak plasma concentration (Cmax X 10) as reported previously (16). The complete medium at 10-fold therapeutic peak plasma concentration (Cmax X 10) as reported previously (16). The complete medium was supplemented with 10% heat-inactivated fetal calf serum (GIBCO, New York, USA), 2 mM L-glutamine and antibiotics (100 U penicillin /ml and 100 µg streptomycin /ml).

**Preparation of samples.** Separation of tumor cells was performed as previously described (12). Briefly, tumor tissues were dissected into pieces smaller than 2 mm³ and immersed in a complete medium containing collagenase (2 mg/ml, Type V-S; Sigma, St. Louis, MO, USA) and Dnase-I (0.4mg/ml; Sigma). After 40 min of incubation at 37°C, the cells were harvested, washed and suspended in a complete medium. The single cell suspension was centrifuged on Ficoll-Hypaque (specific gravity 1.077; Pharmacia, Uppsala, Sweden) gradients at 400 g for 30 min. The interface was collected and suspended at a density of 1 X 10^6 /ml in a complete medium. The cells were then layered on discontinuous gradients consisting of 10 ml of 100% and 15 ml of 75% Ficoll-Hypaque. After centrifugation at 400 g for 30 min, a tumor cell-rich fraction was collected from the 75% interface. The tumor cell-rich suspension was then layered onto discontinuous gradients containing 4 ml each of 25%, 15% and 10% Percoll (Pharmacia) in a complete medium. Centrifugation was performed at 25 g for 7 min. Tumor cells depleted of lymphoid cells were collected from the bottom and from the 25% interface and suspended in a complete medium at a density of 1 X 10^6 /ml. The cells thus prepared were primarily tumor cells, with less than 10% contamination of non-malignant cells as judged by morphological and immunohistochemical examination. Tumor cells were more than 90 - 95% viable by the trypan blue dye exclusion test.

**MMT assay.** Chemosensitivity tests were assessed using the tetrazolium salt MTT (Sigma No. M2128) to measure the viability of tumor cells, as previously described (13, 14). After a 96-h incubation with tumor cells and anticancer drugs, an MTT solution was added and the plates were read on a microplate reader (Corona Electric, MTP-32) using a test wavelength of 570 nm and a reference wavelength of 630 nm. The control wells without tumor cells had an OD of less than 0.005. Samples in which the OD was over 0.1 were accepted for the assay. The inhibition rate was calculated as follows:

\[
\text{Inhibition rate} = \left( \frac{1-\text{OD drug treated}}{\text{OD control}} \right) \times 100
\]

The background of tumor cells (including dead cells) without the addition of MTT had an OD of less than 0.012 after a 96-h incubation, therefore the influence of dead cells was ignored in the present study. The viability of tumor cells was maintained at 75-90% during the 96-h incubation. The drugs with an inhibition rate greater than 70% were considered to be sensitive in vitro according to our preliminary studies (12, 13).

**Statistical analysis.** Quantitative results were expressed as mean±standard deviation of the mean. Significant differences were determined by Fisher’s PLSD test or a Chi-square test. A p value of less than 0.05 was considered to be statistically significant.

**Results**

**Chemosensitivity of gastric cancer.** During the study period, a total of 485 lesions with gastric cancer were tested by an MTT assay. Four hundred and seventy-one lesions were considered to be evaluable (success rate: 97.1%). Table I shows the overall results of chemosensitivity for each drug. The inhibition rates of tumor cells for CDDP and 5-FU were significantly higher than those for MMC and ADR. The inhibition rate and efficacy rate for VP-16 were significantly lower than those for other drugs. The inhibition rate for DOC was equivalent to those for CDDP and 5-FU, although the estimated efficacy rate for DOC was lower than those for CDDP and 5-FU.

**Comparison of chemosensitivity between primary tumors and metastatic tumors.** We compared the chemosensitivity of the primary tumor to that of metastatic lesions including liver metastasis, lymph node metastasis, malignant ascites and ovarian metastasis in the same patient. The inhibition rates and efficacy rates for CDDP, 5-FU and VP-16 of the metastatic tumors were significantly lower than those of the primary lesions respectively (Table II).

**Clinicopathological characteristics and chemosensitivity.** The co-relation of the clinicopathological characteristics with chemosensitivity was investigated. No statistically significant
difference of inhibition rate or efficacy rate between differentiated tumors and undifferentiated tumors was observed for any drug (Table III). Tumors were classified into two groups of non-invasive and invasive type tumors according to the guidelines of the Japanese Gastric Cancer Association. The inhibition rates and efficacy rates for VP-16 and CPT-11 in invasive type tumors were lower than those in non-invasive type tumors. On the other hand, the inhibition rate and efficacy rate for DOC in invasive type tumors were higher than those in non-invasive type tumors. There was no significant difference in the inhibition rates and efficacy rates for other drugs between non-invasive and invasive type tumors, although the efficacy rate for 5-FU in invasive type tumors tended to be low compared with that in non-invasive type tumors (Table IV).

We classified tumors into two groups according to the depth of invasion. The inhibition rate and efficacy rate for VP-16 in cases with serosal invasion were lower than those in cases without serosal invasion. There was no statistical difference between the inhibition rates and efficacy rates for other drugs in cases with serosal invasion and those in cases without serosal invasion (Table V).

Clinical stage and chemosensitivity. We compared the inhibition rates and efficacy rates of the patients with stage I, II and III to those of the patients with stage IV. The inhibition rates and efficacy rates for 5-FU, VP-16 and DOC in stage IV were lower than those in stages I, II and III. The inhibition rates and efficacy rates for CDDP and CPT-11 in stage IV tended to be lower than those in stages I, II and III, although there was no statistical difference. The inhibition rates and efficacy rates for MMC and ADR in stages I, II and III were equivalent to those in stage IV, although the efficacy rate for ADR in stage IV tended to be high compared with those in stages I, II and III (Table VI).

Discussion

We analyzed the results of chemosensitivity using an MTT assay in 435 consecutive gastric cancer patients. Based on the overall results, CDDP and 5FU showed higher sensitivities than MMC, ADM and VP-16. This is in agreement with previous reports (17, 18). Both CDDP and 5FU are now key drugs in chemotherapy for gastric cancer. On the other hand, VP-16 showed a lower sensitivity than other drugs, suggesting that VP-16 alone is not effective for most gastric cancer. Although a combined chemotherapy, such as EAP therapy, has previously been applied (19). CPT-11 also showed a low inhibition and efficacy rate in the same way, suggesting that CPT-11 alone is also not effective.

Table I. Chemosensitivity of gastric cancer.

<table>
<thead>
<tr>
<th>Drug</th>
<th>CDDP (n=462)</th>
<th>MMC (n=458)</th>
<th>ADR (n=459)</th>
<th>5-FU (n=451)</th>
<th>VP-16 (n=100)</th>
<th>CPT-11 (n=140)</th>
<th>DOC (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibition rates (%)</td>
<td>68.1±22.2a</td>
<td>64.2±23.0</td>
<td>64.7±23.1</td>
<td>66.4±23.1</td>
<td>44.7±26.3b</td>
<td>55.1±22.6</td>
<td>67.4±22.3</td>
</tr>
<tr>
<td>Efficacy rates (%)</td>
<td>55.6 (257/462)a</td>
<td>46.9 (215/458)</td>
<td>47.9 (220/459)</td>
<td>54.1 (244/451)</td>
<td>19.0 (19/100)b</td>
<td>29.3 (41/140)</td>
<td>49.3 (35/71)</td>
</tr>
</tbody>
</table>

a < 0.05, compared with the inhibition rates and efficacy rates for MMC and ADR.
b < 0.01, compared with those for other drugs.

Table II. Comparison of chemosensitivity between primary tumors and metastatic tumors.

<table>
<thead>
<tr>
<th>Drug</th>
<th>CDDP</th>
<th>MMC</th>
<th>ADR</th>
<th>5-FU</th>
<th>VP-16</th>
<th>CPT-11</th>
<th>DOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary lesions Inhibition rates (%)</td>
<td>69.1±21.6</td>
<td>64.9±22.5</td>
<td>64.3±22.6</td>
<td>68.7±21.7</td>
<td>50.9±23.6</td>
<td>56.4±22.4</td>
<td>69.2±20.6</td>
</tr>
<tr>
<td>Efficacy rates (%)</td>
<td>58.3 (211/362)</td>
<td>47.8 (171/358)</td>
<td>47.8 (171/358)</td>
<td>58.1 (204/351)</td>
<td>22.5 (16/71)</td>
<td>29.6 (32/108)</td>
<td>53.3 (32/60)</td>
</tr>
<tr>
<td>Metastatic lesions Inhibition rates (%)</td>
<td>62.6±25.0a</td>
<td>60.3±25.2</td>
<td>67.3±25.8</td>
<td>54.3±29.1b</td>
<td>27.3±25.9b</td>
<td>50.0±23.4</td>
<td>57.6±29.2</td>
</tr>
<tr>
<td>Efficacy rates (%)</td>
<td>46.4 (32/69)a</td>
<td>42.6 (29/68)</td>
<td>52.2 (35/67)</td>
<td>32.9 (23/70)b</td>
<td>11.5 (3/26)b</td>
<td>25.0 (7/28)</td>
<td>27.3 (3/11)</td>
</tr>
</tbody>
</table>

a < 0.05, compared with the inhibition rate and efficacy rate of primary lesions.
b < 0.01, compared with those of primary lesions.
for most gastric cancer. It is interesting that the inhibition rate for DOC was equivalent to those for CDDP and 5-FU, but the efficacy rate was lower than those for CDDP and 5-FU, meaning patients who are sensitive to DOC are fewer than those sensitive to CDDP and 5-FU, although the average sensitivity for DOC is considered to be equivalent to those of CDDP and 5-FU. These results suggested that DOC should be used in a combined chemotherapy for gastric cancer (20).

In the present study, chemosensitivity in metastatic lesions was lower than that in primary lesions. Our results were consistent with those of a previous report (21). In metastatic lesions, as micro environments of cancer cells are changed, the chemosensitivity of metastatic lesions may change from that of the primary lesions (22). Therefore, if possible, chemosensitivity testing should be performed not only in primary lesions, but also in metastatic lesions. However, it is usually difficult to obtain tumor cells both from the primary lesion and metastatic lesion. We have to give careful consideration to the differences of chemosensitivity between the primary and metastatic lesions because it is of the utmost importance to control metastatic lesions in the treatment of advanced gastric cancer.

Clinicopathological findings, such as tumor differentiation, macroscopic appearance and depth of invasion, were not correlated with chemosensitivity in most drugs. Our results are not consistent with previous reports (23-25). In this study, more than 450 lesions were analyzed for sensitivity to CDDP, MMC, ADM and 5-FU. Therefore, our data is more reliable than that of prior reports. There was a great variety of sensitivity for these drugs and the correlation to clinicopathological findings was not recognized for these drugs at all. These results suggest that it is difficult to predict the appropriate chemotherapies for gastric cancer according to the clinicopathological findings of the tumors. On the other hand, the chemosensitivity to some drugs, such as VP-16, CPT-11 and DOC, can to be predicted by macroscopic appearance. VP-16 and CPT-11 showed lower sensitivities in tumors of an invasive type rather than those of a non-invasive type, while DOC showed higher sensitivity in those of an invasive type rather than in those of a non-invasive type. CPT-11 especially showed a high sensitivity in both differentiated tumors and tumors of a non-invasive type, consistent with previous reports (26). The difference between invasive and non-invasive type tumors is described as the difference of the manner of

| Table III. Comparison of chemosensitivity between differentiated and undifferentiated tumors. |
|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| CDDP ММС ADR 5-FU VP-16 CPT-11 DOC               | CDDP ММС ADR 5-FU VP-16 CPT-11 DOC               | CDDP ММС ADR 5-FU VP-16 CPT-11 DOC               | CDDP ММС ADR 5-FU VP-16 CPT-11 DOC               | CDDP ММС ADR 5-FU VP-16 CPT-11 DOC               | CDDP ММС ADR 5-FU VP-16 CPT-11 DOC               |
| Differentiated tumors                            | Inhibition rates (%) 69.0±19.3 63.3±20.9 64.0±19.8 70.3±21.4 52.2±23.4 56.2±21.5 66.7±21.4 | Efficacy rates (%) 54.8 (85/155) 42.6 (66/155) 43.9 (68/155) 60.5 (92/152) 19.4 (6/31) 30.9 (17/55) 38.7 (12/31) | Differentiated tumors                            | Inhibition rates (%) 68.6±23.2 65.0±23.9 65.0±24.4 65.9±24.9 41.0±27.5 53.0±23.0 65.8±23.4 | Efficacy rates (%) 59.6 (118/198) 49.0 (97/198) 49.2 (97/197) 53.6 (105/196) 15.0 (6/40) 24.6 (15/61) 52.8 (19/36) |
| Undifferentiated tumors                          | Inhibition rates (%) 68.6±23.2 65.0±23.9 65.0±24.4 65.9±24.9 41.0±27.5 53.0±23.0 65.8±23.4 | Efficacy rates (%) 59.6 (118/198) 49.0 (97/198) 49.2 (97/197) 53.6 (105/196) 15.0 (6/40) 24.6 (15/61) 52.8 (19/36) |
| Differentiated tumors include tubular and papillary adenocarcinoma. | Undifferentiated tumors include poorly-differentiated adenocarcinoma and signet ring cell carcinoma. |

Table IV. Chemosensitivity and macroscopic appearance.

<table>
<thead>
<tr>
<th>CDDP ММС ADR 5-FU VP-16 CPT-11 DOC</th>
<th>CDDP ММС ADR 5-FU VP-16 CPT-11 DOC</th>
<th>CDDP ММС ADR 5-FU VP-16 CPT-11 DOC</th>
<th>CDDP ММС ADR 5-FU VP-16 CPT-11 DOC</th>
<th>CDDP ММС ADR 5-FU VP-16 CPT-11 DOC</th>
<th>CDDP ММС ADR 5-FU VP-16 CPT-11 DOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive type tumors</td>
<td>Inhibition rates (%) 70.9±19.6 63.1±23.0 64.6±21.3 73.8±19.1 65.6±20.4 60.8±18.8 56.8±22.5</td>
<td>Efficacy rates (%) 61.2 (37/60) 46.6 (27/58) 43.3 (26/60) 67.8 (40/59) 42.9 (3/7) 31.8 (7/22) 23.1 (3/13)</td>
<td>Invasive type tumors</td>
<td>Inhibition rates (%) 69.1±20.6 64.9±22.1 62.8±23.4 68.5±22.9 44.6±25.4a 50.2±21.5a 71.0±18.8a</td>
<td>Efficacy rates (%) 54.2 (83/153) 48.3 (73/151) 47.3 (71/150) 57.0 (86/151) 10.3 (3/29)a 18.2 (8/44)a 57.7 (15/26)a</td>
</tr>
<tr>
<td>Invasive type tumors</td>
<td>Inhibition rates (%) 70.9±19.6 63.1±23.0 64.6±21.3 73.8±19.1 65.6±20.4 60.8±18.8 56.8±22.5</td>
<td>Efficacy rates (%) 61.2 (37/60) 46.6 (27/58) 43.3 (26/60) 67.8 (40/59) 42.9 (3/7) 31.8 (7/22) 23.1 (3/13)</td>
<td>Invasive type tumors</td>
<td>Inhibition rates (%) 69.1±20.6 64.9±22.1 62.8±23.4 68.5±22.9 44.6±25.4a 50.2±21.5a 71.0±18.8a</td>
<td>Efficacy rates (%) 54.2 (83/153) 48.3 (73/151) 47.3 (71/150) 57.0 (86/151) 10.3 (3/29)a 18.2 (8/44)a 57.7 (15/26)a</td>
</tr>
<tr>
<td>Invasive type tumors</td>
<td>Inhibition rates (%) 70.9±19.6 63.1±23.0 64.6±21.3 73.8±19.1 65.6±20.4 60.8±18.8 56.8±22.5</td>
<td>Efficacy rates (%) 61.2 (37/60) 46.6 (27/58) 43.3 (26/60) 67.8 (40/59) 42.9 (3/7) 31.8 (7/22) 23.1 (3/13)</td>
<td>Invasive type tumors</td>
<td>Inhibition rates (%) 69.1±20.6 64.9±22.1 62.8±23.4 68.5±22.9 44.6±25.4a 50.2±21.5a 71.0±18.8a</td>
<td>Efficacy rates (%) 54.2 (83/153) 48.3 (73/151) 47.3 (71/150) 57.0 (86/151) 10.3 (3/29)a 18.2 (8/44)a 57.7 (15/26)a</td>
</tr>
</tbody>
</table>

*p<0.05, compared with the inhibition rates and efficacy rates of non-invasive type tumors.

According to the guideline of the Japanese Gastric Cancer Association, tumors were classified into non-invasive and invasive type tumors by macroscopic appearance.
tumor growth by infiltration or expansion (27). Tumor vascularity and fibrosis are also different in these types of tumors. Therefore, these factors may affect the chemosensitivity to some kinds of drugs.

We compared the chemosensitivities between cases in stages I, II and III with that of stage IV cases. The chemosensitivity of stage IV cases was generally lower than those of stage I, II and III cases. This may be because of the effect of previous chemotherapy. In stage IV cases, tumor cells could acquire a tolerance for anti-cancer drugs, which were administered before and, therefore, we should select drugs that are not influenced by prescribed chemotherapy. Chemosensitivity tests could play an important role in selecting a regimen of second-line chemotherapy. We have also tested the sensitivity of paclitaxel (PTX) in stage IV cases because PTX does not show a cross-resistance to CDDP and 5-FU (data not shown). PTX showed a higher sensitivity in stage IV cases than in stage I, II and III cases. This is contrary to the results of other drugs, suggesting that PTX is a good candidate for second-line chemotherapy for gastric cancer (28).

Furthermore, we have often experienced a change in the chemosensitivity of a patient as the clinical stage progresses. Therefore chemosensitivity, even in the same patient, should be assessed as frequently as possible.

It is reasonable to state that chemotherapy is of benefit to patients with advanced gastric cancer, but the extent of this benefit is limited, and there appears to be no standard, universally accepted regimen. Recently, new anticancer drugs such as S-1, paclitaxel and docetaxel have been developed, and are already available for gastric cancer. In particular, S-1 has been reported to be very effective in phase II clinical trials (29). However, the efficacy rates of these drugs are less than 50% and adverse effects can not be ignored. The chemosensitivity of each patient to different drugs varies greatly, so it makes no sense to analyze the chemosensitivity of a group. Although chemotherapeutic regimens for cancer patients are usually based on the statistical results of clinical trials, in order to prolong overall survival of advanced gastric cancer patients by chemotherapy, the standard regimen should be established according to individual chemosensitivity. Furthermore, adverse effects could be

Table V. Chemosensitivity and depth of invasion.

<table>
<thead>
<tr>
<th>Serosal invasion</th>
<th>CDDP Inhibition rates (%)</th>
<th>MMC Inhibition rates (%)</th>
<th>ADR Inhibition rates (%)</th>
<th>5-FU Inhibition rates (%)</th>
<th>VP-16 Inhibition rates (%)</th>
<th>CPT-11 Inhibition rates (%)</th>
<th>DOC Inhibition rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>68.9±20.8</td>
<td>61.9±19.3</td>
<td>64.7±18.0</td>
<td>73.4±16.4</td>
<td>63.4±18.4</td>
<td>53.7±21.1</td>
<td>68.4±22.4</td>
</tr>
<tr>
<td>Efficacy rates (%)</td>
<td>51.6 (36/62)</td>
<td>39.3 (24/61)</td>
<td>44.3 (27/61)</td>
<td>62.3 (38/61)</td>
<td>36.4 (4/11)</td>
<td>21.4 (6/28)</td>
<td>55.6 (10/18)</td>
</tr>
<tr>
<td>Yes</td>
<td>69.3±20.6</td>
<td>64.9±23.0</td>
<td>62.9±23.9</td>
<td>68.5±23.3</td>
<td>42.9±25.7a</td>
<td>55.0±20.6</td>
<td>65.0±22.4</td>
</tr>
<tr>
<td>Efficacy rates (%)</td>
<td>54.4 (86/158)</td>
<td>49.7 (77/155)</td>
<td>46.8 (73/156)</td>
<td>57.7 (90/156)</td>
<td>7.7 (2/26)a</td>
<td>23.8 (10/42)</td>
<td>40.0 (10/25)</td>
</tr>
</tbody>
</table>

*p<0.05, compared with the inhibition rate and efficacy rate of the cases without serosal invasion.

According to the microscopic findings, tumors were classified into with serosal invasion (Yes) or without serosal invasion (No).

Table VI. Chemosensitivity and clinical stage.

<table>
<thead>
<tr>
<th>Stage</th>
<th>CDDP Inhibition rates (%)</th>
<th>MMC Inhibition rates (%)</th>
<th>ADR Inhibition rates (%)</th>
<th>5-FU Inhibition rates (%)</th>
<th>VP-16 Inhibition rates (%)</th>
<th>CPT-11 Inhibition rates (%)</th>
<th>DOC Inhibition rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I, II, III</td>
<td>70.6±19.5</td>
<td>63.9±22.6</td>
<td>64.0±21.5</td>
<td>69.6±21.8</td>
<td>55.8±22.3</td>
<td>58.1±21.4</td>
<td>73.6±22.6</td>
</tr>
<tr>
<td>Efficacy rates (%)</td>
<td>57.9 (103/178)</td>
<td>45.6 (82/180)</td>
<td>42.8 (77/180)</td>
<td>59.4 (104/175)</td>
<td>26.7 (8/30)</td>
<td>32.2 (19/59)</td>
<td>64.7 (22/34)</td>
</tr>
<tr>
<td>Stage IV</td>
<td>66.7±23.0</td>
<td>64.5±22.3</td>
<td>65.5±23.5</td>
<td>63.9±25.4a</td>
<td>37.8±27.3b</td>
<td>52.9±22.7</td>
<td>60.4±20.4a</td>
</tr>
<tr>
<td>Efficacy rates (%)</td>
<td>55.1 (113/205)</td>
<td>46.8 (95/203)</td>
<td>51.2 (104/203)</td>
<td>49.5 (101/204)a</td>
<td>14.3 (7/49)b</td>
<td>27.1 (19/70)</td>
<td>31.4 (11/35)a</td>
</tr>
</tbody>
</table>

*p<0.05, compared with the inhibition rates and efficacy rates of Stage I, II and III.

The clinical stage of the patients was determined according to TNM classification.
avoided by being aware of individual chemosensitivities. This could lead to an improvement in the quality of life for gastric cancer patients. Therefore, chemosensitivity testing is essential for individualized chemotherapy.

Cytosensitivity testing has not been approved by social insurance agencies in Japan (30). Now is the time to summarize the cumulative results of chemosensitivity testing and to clarify the advantage of chemosensitivity testing for cancer treatment. Chemosensitivity prediction may indeed be feasible to achieve the goal of personalized medicine in gastric cancer.

In conclusion, there is a great variety of sensitivities to anticancer drugs in each patient and it is difficult to predict the appropriate anticancer drug according to the clinicopathological findings of tumors. The chemosensitivity is different between primary and metastatic lesions and changes as the clinical stage progresses in the same patient. Chemosensitivity testing is one of the most effective strategies for predicting an appropriate anticancer regimen. Furthermore, chemotherapy based on the results of chemosensitivity testing could be useful in terms of avoiding of uncomfortable adverse effects and would have economic advantages.

References


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