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Efficacy and feasibility of S-1/low dose CDDP in patients with unresectable or recurrent gastric cancer

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Background: Chemotherapy confers a survival benefit to patients with unresectable or recurrent gastric cancer, compared with best supportive care alone, but a standard chemotherapy regimen has not yet been established. S-1 is a novel oral fluoropyrimidine derivative consisting of tegafur and two modulators, gemestat and otastat potassium. A previous phase II study showed that S-1 was effective for the treatment of advanced gastric cancer with mild toxicity. In a Phase I/II study of S-1 combined with cisplatin, the response rate was 74% (14/19), and the median survival period was 383 days.
Unfortunately, this regimen had a high incidence of severe (grade 3–4) toxicities. Thus, it is presently difficult to use this regimen in clinically. In this study, we treated patients with unresectable and recurrent gastric cancer using a new regimen, S-1 combined with a low dose CDDP regimen, to reduce the non-hematological adverse effects.
Purpose: To evaluate the efficacy and feasibility of S-1/low dose CDDP for the treatment of patients with unresectable or recurrent gastric cancer.
Patients and Methods: Fifty patients with unresectable or recurrent gastric cancer were enrolled in this study. S-1 was orally administered twice daily at a dose of 80 mg/m^2/day for 3 weeks, and CDDP (6 mg/m^2) was simultaneously administered 3 times on 5 separate days, each followed by a 2-day interval. This regimen was repeated every 35 days if no disease progression or severe adverse reactions occurred and if the patient was willing to continue treatment.
Results: The incidences of severe (grade 3–4) hematological and non-hematological toxicities were 22% and 2%, respectively. The overall response rate was 62% (31/50). Complete responses were obtained in six patients, and partial responses were obtained in 25 patients. The median survival period was 13.4 months, and the 1-year survival rate was 52%.
Conclusion: This regimen was considered active with acceptable toxicities in patients with unresectable or recurrent gastric cancer.

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The combined operations on the organs of gastro-intestinal tract with an extensive one-stage resection of liver

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Introduction: The majority of resections of liver are carried out at its metastatic affection. The question that is still under discussion nowadays is on necessity of division of surgical intervention: as the first stage the origin is removed, and as the second stage (normally in 2–3 months) the resection of liver is carried out. Most of the authors suggesting the given approach explain it with the high traumaticity of the one-stage surgical intervention. With the development of modern surgery and medicine it becomes possible to carry out the expanded and combined surgical intervention with an extensive one-stage resection of liver.
Purpose: of the given work is the assess of our experience in the combined operations on the organs of gastro-intestinal tract and abdominal cavity with an extensive simultaneous resection of liver.
Materials and methods: In the period since January 1994 till May 2005 the authors of the given work executed 295 surgical interventions on liver, including 68 combined resections of liver. In the same period of time the resection of liver as the second stage of the surgical intervention was executed at 31 patients. The estimated pathology was: cancer of esophagus, stomach cancer, colon cancer, "gynecologic" cancer, abdominal sarcoma, tumors of an adrenal gland, pancreatic cancer, kidney cancer. Both groups of the appraised patients were similar statistically on the majority of parameters. The volume of the resection of liver made not less than 2 segments on Couinaud (max up to 6 segments). The resection of the initial tumor was carried out under oncological principles.
Results: Under all appraised parameters (the multivalent multifactor analysis) we have not received any statistical differences between two groups, including such estimated factors as postoperative death, postoperative complications (quantitative and qualitative criteria), and the duration of hospital stay. The only significant difference between two groups was the duration of surgical intervention (considerably less for two-stage operations). However summarizing the duration of two operations and also all possible complications, bed-days, etc. in the group of two-stage operations we can come to the conclusion that all these parameters will be worse for this particular group comparing with the situation with one-stage surgical interventions.
Conclusion: The received data allow us to assert, that using modern achievements in medicine, surgery and anesthesiology it is possible to carry out extensive combined operations on the organs of gastro-intestinal tract and abdominal cavity with one-stage resection of liver safely in any age group and with the good remote results.

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Dose-response relationship of proton beam therapy for hepatocellular carcinoma

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Background: We have shown that proton beam therapy is an effective and safe treatment method for hepatocellular carcinoma (HCC) regardless of tumor size, number of tumors, or presence or absence of vascular invasion. To evaluate the dose-response relationship of proton beam therapy, we reviewed HCC patients who were treated by proton beam therapy alone.
Patients and methods: From January 1993 through July 2000, 79 HCC patients having 84 HCC lesions, who were initially treated with proton beam therapy alone, were analyzed in terms of local control, survival rates and treatment sequelae. Total doses of 50–81 Gy in 10–27 fractions over 14–47 days (median 72 Gy in 16 fractions over 28 days) were delivered to the tumors. Equivalent doses with 2 Gy per fractions were calculated using linear quadratic model with a/b ratio of 10 and 3 to compare various regimens.
Results: The local control rate at 5 years for all the 84 HCC lesions in 79 patients was 88.5%. Dose-response relationship was not found according to the equivalent dose. The survival rate at 5 years for all of the 79 patients was 27.5%. Degree of impairment in the liver functions and the number of tumors were prognostic factors affecting survival. The five-year survival rate for patients with the least impaired liver functions and a solitary HCC was 58.4%. No patients had a treatment-related toxicity of grade III or more.
Conclusion: Dose-response relationship was not found in this study. Proton beam therapy alone appears effective and safe for patients with HCC. It should be investigated if total doses for the patients could be reduced in the range of 50–81 Gy in 10–27 fractions.

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Preliminary results of proton beam therapy for hepatocellular carcinoma with portal vein tumor thrombus

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Background: Prognosis of advanced hepatocellular carcinoma (HCC) with portal vein tumor thrombus (PVTT) is extremely poor. An optimal treatment strategy is yet to be established. We retrospectively reviewed 23 patients having HCC with PVTT treated with proton beam therapy to explore its potential role.
Material and Methods: From February 1991 to June 2004, 303 patients with HCC were treated with proton beam therapy at University of Tsukuba. Of these, 23 patients had tumor thrombus in the main trunk or major branches of the portal vein. A median total dose of 66 Gy in 22 fractions over 31 days was given to the clinical target volumes, which encompassed the primary tumors and PVTT.
Results: All but two patients had locally controlled tumors during a median follow-up period of 11 months ranging from 2 to 88 months. One of the two patients had a progressive tumor during and after the treatment and died of it 2 months after the beginning of the proton beam therapy. The remaining one successfully underwent a repeated proton beam therapy for a local recurrence or a residual tumor in the boundary of the irradiated volume 1 month after the first course. Twelve patients died and the remaining 11 were alive as of March 2005. Of the 12 patients dead 7 died of multiple tumors in the liver, 3 died of distant metastases, and 1 died of the primary tumor that progressed during and after proton beam therapy. The 2-year survival and the median survival period for the 23 patients were 58% and 27 months, respectively. A treatment related-toxicity of grade 3 or more was not observed.
Conclusions: Proton beam therapy for HCC with PVTT is effective and feasible. It appears to significantly improve local control and prolong survival for the patients.