Preoperative neoadjuvant chemoradiation for locally advanced gastric adenocarcinoma

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ABSTRACT

AIMS AND BACKGROUND: To evaluate toxicity and the radical resection rate in gastric adenocarcinoma treated with preoperative neoadjuvant chemoradiation.

MATERIALS & METHODS: 32 patients, 22 males and 10 females with gastric adenocarcinoma, were treated with chemoradiation and hyperthermia.

RESULTS: The neoadjuvant regimen was completed as planned in 19/32 (59 %) patients; in the remaining patients the intensity of chemotherapy had to be reduced because of haematological and gastrointestinal toxicity. Surgical stage was as follows: 2 patients pathologically complete response, 3 patients AJCC stage I.A, 5 patients stage I.B, 7 patients stage II, 7 patients stage III.A, 1 patient stage III.B, 7 patients stage IV. R0 resection was achieved in 19/32 (59%) patients, R1 in 2/32 (6%) patients and R2 in 11 (34%) patients. Downstaging after neoadjuvant chemoradiotherapy was achieved in 17/32 (53%) patients. At the date of evaluation (31 March 2009), 4 patients were still alive 58, 81, 86 and 98 months from the date of diagnosis. Median survival was 18 months (95% confidence interval: 13–38 months). One-year survival was 69% (95% confidence interval: 53%–85%). Four-year survival was 19% (95% C.I.: 5%–34%).

CONCLUSIONS: Preoperative neoadjuvant chemoradiotherapy has acceptable toxicity, and can lead to a high rate of R0 resections.

KEY WORDS: gastric cancer, preoperative neoadjuvant chemoradiotherapy, hyperthermia

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BACKGROUND

The mainstay of curative treatment of locally advanced gastric adenocarcinoma is radical surgery. Complete surgical tumour removal with microscopically negative margins (R0 resection) is of fundamental importance for the patient's prognosis. Locoregional relapse is a major problem after curative surgery in gastric adenocarcinoma.

Preoperative neoadjuvant chemoradiotherapy has been widely used in the treatment of locally advanced oesophageal and rectal adenocarcinoma, but studies in gastric adenocarcinoma are limited.

Unsatisfactory results of surgery alone in locally advanced gastric adenocarcinoma have led to an increased interest in adjuvant or neoadjuvant therapeutic approaches. According to a meta-analysis published by Hu in 2002, intravenous adjuvant chemotherapy after gastrectomy may have a positive effect on the outcome in gastric cancer [1]. However, the evidence is not strong because of the generally low methodological quality of most of the randomized trials of adjuvant chemotherapy. The principal aim of neoadjuvant therapy is to enable the surgeon to achieve radical resection with microscopically negative margins (R0 resection). Preoperative radiotherapy in gastric cancer has been tested in several non-randomized [2, 3, 4, 5] and randomized studies [6, 7, 8].

AIM

The aim of the present retrospective analysis was to evaluate toxicities and the rate of radical resection with microscopically negative margins (R0 resection) in gastric adenocarci-

noma treated according to a protocol of preoperative neoadjuvant chemoradiation.

MATERIALS & METHODS

Patients

Between March 1999 and December 2003, 32 patients, 22 males and 10 females, median age 63 (range 28–80) years, with gastric adenocarcinoma were treated with neoadjuvant chemoradiation at the Department of Oncology and Radiotherapy, Charles University Medical School Teaching Hospital in Hradec Králové. Initial examinations included case history, physical examination, blood count, biochemistry, lung X-rays, abdominal US, gastroscopy, spiral abdominal contrast CT, endosonography, and endobiopsy. Staging was based on AJCC classification [9]. All patients had histology of adenocarcinoma: 1 patient grade 1, 10 patients grade 2, 17 patients grade 3 and 4 patients grade 4. Pre-treatment stage was as follows: 1 patient AJCC stage I.B, 12 patients stage II, 15 patients stage III.A and 4 patients stage IV.

Anatomical localization of the tumour was as follows: cardia 8 patients, body 6 patients, antrum 5 patients, pylorus 1 patient, lesser curvature 4 patients and greater curvature 8 patients. The median of pre-treatment haemoglobin level was 131 (range 92–163) g/l, leucocytes 7.4 (range 3.2–11.6) 10^9/l and thrombocytes 260 (range 122–438) 10^9/l.

Toxicity was evaluated according to the Common Toxicity Criteria for Adverse Events version 3.0.

Treatment

The following regimens of chemoradiation were used: two 3-week cycles of 5-fluorouracil (5-FU) 200 mg/m^2 continuously days 1–21 with calcium folinate 45 mg per day, cisplatin 25 mg/m^2 days 1, 8, 15, paclitaxel 60 mg/m^2 days 1, 8, 15 and concomitant radiotherapy 30 Gy in 15 fractions (2 Gy daily) of stomach and regional nodes (10 patients; completed in 5/10 patients), in 6/10 patients combined with ultrasound hyperthermia once weekly during the second cycle of chemotherapy (completed in 2/6 patients); 5-FU 200 mg/m^2 continuously 4 weeks and cisplatin 25 mg/m2 days 1, 8, 15, 22, paclitaxel 60 mg/m2 days 1, 8, 15, 22 and concomitant radiotherapy 40 Gy in 20 fractions (2 Gy daily) of stomach and regional nodes (5 patients; completed in 1/5 patients), in 2/5 patients combined with ultrasound hyperthermia once weekly (completed in all patients); 5-FU 200 mg/m^2 continuously 3 weeks and cisplatin 25 mg/m^2 days 1, 8, 15 and concomitant radiotherapy 30 Gy in 15 fractions (2 Gy daily) of stomach and regional nodes (7 patients; completed in 5/7 patients); 5-FU 200 mg/m2 continuously 4 weeks and cisplatin 25 mg/m2 days 1, 8, 15, 22 and concomitant radiotherapy 40 Gy in 20 fractions (2 Gy daily) of stomach and regional nodes (3 patients; completed in all patients); 5-FU 200 mg/m^2 continuously 4 weeks and concomitant radiotherapy 40 Gy in 20 fractions (2 Gy daily) of stomach and regional nodes (7 patients; competed in 5/7 patients). Surgery was performed within 5 weeks after completion of chemoradiotherapy. It consisted of gastrectomy with lymphadenectomy. Histological examination of the resected tissue with lymphatic block and surrounding lymph nodes was performed.

Radiation therapy

External beam radiation was administered concomitantly with the second cycle of chemotherapy.

Radiotherapy with two conformal radiation fields, anterior-posterior and posterior-anterior, involved the entire stomach with perigastric extension and major lymph nodes at risk. Fields were individually modified as it was necessary to spare as much normal tissue as possible, and to shield at least one wholly functional kidney in summation. Function of kidneys was initially evaluated by dynamic scintigraphy. The scheduled dose of radiation was delivered by a linear accelerator (Clinac 600 or Clinac 2100, Varian Medical Systems, Palo Alto, CA, U.S.A.) using 6-MV or 15-MV photons. Radiotherapy was delivered 5 days per week and covered every radiation field. A total dose of 30 Gy in 15 fractions was planned in 17 patients (in 1 of 17 patients the dose had to be reduced because of the haematological and gastrointestinal toxicity of chemoradiotherapy) and 40 Gy in 20 fractions in 15 patients (in 4 of 15 patients the dose had to be reduced because of the haematological and gastrointestinal toxicity of chemoradiotherapy).