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Postoperative radiation and concomitant bolus fluorouracil with or without additional chemotherapy with fluorouracil and high-dose leucovorin in patients with high-risk rectal cancer: a randomized phase III study conducted by the Hellenic Cooperative Oncology Group.

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Source

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Abstract

BACKGROUND:

Randomized studies have shown that postoperative chemotherapy with or without radiation therapy (RT) improved local control and survival of patients with stages II or III rectal cancer. However, the optimal sequence of treatments and the optimal chemotherapeutic regimen have not been defined. Modulation of fluorouracil (FU) by leucovorin (LV) has yielded a highly significant difference in response rate from that of FU monotherapy, as suggested by an overview of randomized trials in patients with advanced colorectal cancer. However, this difference in response rate did not translate into a survival benefit.

PURPOSE:

To evaluate the impact on the disease-free survival (DFS) and overall survival (OS) of patients with stages II or III rectal cancer of postoperative RT and concomitant bolus FU administration alone or with additional chemotherapy using FU and high-dose LV.

PATIENTS AND METHODS:

From October 1989 until February 1997, 220 patients were randomized postoperatively to receive either one cycle of chemotherapy with FU (600 mg/m2/week x 6 followed by a two-week rest) and leucovorin (LV, 500 mg/m2/week x 6 as a two-hour infusion) followed by pelvic RT with concomitant FU (400 mg/m2) as a rapid intravenous injection during the first three and last three days of RT, and three more cycles of the same chemotherapy with FU and LV (standard, group A, 111 patients) or pelvic RT with concomitant FU only (experimental, group B, 109 patients).

RESULTS:

As of August 1998, after a median follow-up of 4.9 years, there was no significant difference in either three-year DFS (Group A, 70.3%; group B, 68.2%, P = 0.53) or OS (group A, 77%; group B, 73.3%. P = 0.75). Cox multivariate analysis revealed stage of disease, number of infiltrated nodes, tumor grade, presence of regional implants and perforation to be significant prognostic factors. The incidence of severe side effects was significantly higher in the patients in group A than in those in group B (32.4% vs. 4.6%, P < 0.0001).

CONCLUSIONS:

The incorporation of additional chemotherapy with FU and LV into postoperative concomitant RT and bolus infusion of FU does not offer a > or = 10% three-year survival benefit over that of concomitant RT and bolus infusion of FU, and significantly increases toxicity in patients with stages II or III rectal cancer.