Regional versus systemic chemotherapy in the treatment of colorectal carcinoma metastatic to the liver: is there a survival difference? Meta-analysis of the published literature

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Authors' objectives
To determine whether delivery of chemotherapy by hepatic artery infusion improves survival of patients with colorectal cancer with liver metastases, relative to systemic chemotherapy.

Searching
MEDLINE was searched from 1991 to 1995. Additional material was obtained by examining references from articles and lists from recent meetings, and by contacting experts in the field. The search was not limited to English language studies.

Study selection
Study designs of evaluations included in the review
Prospective randomised trials which reported length of survival were included.

Specific interventions included in the review
5-fluorouracil (5-FU) or floxuridine (FUDR), either administered directly to the liver by hepatic artery infusion, or given systemically.

Participants included in the review
Patients with metastatic colorectal cancer, confined to the liver and confirmed by biopsy, were included.

Outcomes assessed in the review
Survival from time of randomisation until death was assessed.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Only studies which made reference to randomisation were included. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The following information was extracted from each study: time period of patient accrual, randomisation details, chemotherapeutic agents used, route of administration, and outcomes measured. One- and 2-year survival rates were calculated for each treatment arm of each study.

Methods of synthesis
How were the studies combined?
Survival was expressed as a percentage at 1 and 2 years after randomisation, using intention to treat. Survival differences between study arms were calculated with 95% confidence intervals (CIs). The data were then combined using a fixed-effect model to obtain summary estimates of survival differences at 1 and 2 years.

How were differences between studies investigated?
Homogeneity of treatment effect was tested using the method of DerSimonian and Laird (see Other Publications of Database of Abstracts of Reviews of Effects (DARE) and Other Publications of Database of Abstracts of Reviews of Effects (DARE)).
Related Interest). No significant differences were detected. In addition, separate analyses were carried out for the 3 studies which did not allow crossover of treatment, and also excluding 1 study in which control group results may have been biased.

**Results of the review**

Six studies (N=579) were included.

Hepatic artery infusion led to a 12.9% improvement in survival at 1 year (95% CI: 4.8, 20.9, p=0.002). The 2-year survival difference was 7.5% (95% CI: 0.9, 14.2, p=0.026). When only those studies that did not allow treatment crossover were included in the analysis, the survival advantage with hepatic regional chemotherapy appeared greater at 1 year, at 19.1% (95% CI: 8, 30.2, p=0.001); after 2 years, the survival difference was 8.6% (95% CI: 0.1, 17.1, p=0.049).

In one study, half of the control group did not actually receive systemic chemotherapy. Re-calcualting summary statistics after excluding that study showed that the advantage of hepatic regional chemotherapy was still significant at 1 year (95% CI: 0.4, 19.5, p=0.041), but not at 2 years (95% CI: -1.8, 14.5, p=0.124).

**Authors' conclusions**

Hepatic artery infusion chemotherapy using FUDR leads to improved survival relative to systemic chemotherapy using either 5-FU or FUDR in patients with colorectal cancer metastatic to the liver. However, the authors believe that current data do not show clinical significance, and that investigators should include quality of life studies in the assessment of the treatment effect.

**CRD commentary**

The authors have taken some trouble to ensure that their conclusions are not biased. This appears to be a reliable meta-analysis.

**Implications of the review for practice and research**

Whether regional chemotherapy to the liver should be offered to patients with isolated liver metastases after curative resection of colorectal cancer may depend on the cost-effectiveness of the procedure. On present evidence, it appears to improve survival in the short-to-medium term.

**Bibliographic details**


**PubMedID**

8859174

**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Colorectal Neoplasms /mortality /pathology; Floxuridine /administration & dosage; Fluorouracil /administration & dosage; Humans; Infusions, Intra-Arterial; Liver Neoplasms /drug therapy /mortality /secondary; Survival Rate;
Treatment Outcome

**AccessionNumber**
11996001716

**Date bibliographic record published**
31/05/1997

**Date abstract record published**
31/05/1997

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.