Management of patients with asymptomatic colorectal cancer and synchronous irresectable metastases

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CRD summary
This review concluded that resection of the primary colorectal tumour provided minimal palliative benefit to patients with stage IV colorectal cancer, can result in major morbidity and mortality and can potentially delay systemic chemotherapy. Given several considerations, including limitations with the search and difficulties with the analysis, it was difficult to determine whether the authors' conclusions are reliable.

Authors' objectives
To compare the effectiveness of surgery versus chemotherapy for the treatment of patients with stage IV colorectal cancer.

Searching
PubMed and The Cochrane Library were searched from 1980 for articles in English. Search terms were reported. References of included studies were searched manually to identify further relevant articles.

Study selection
Studies reporting a series of patients with stage IV colorectal cancer (incurable colorectal cancer) who had undergone surgery (resection) of the primary colorectal tumour or who were treated with systematic chemotherapy were included in the review. The outcomes of interest were complications, response and/or survival data.

Most studies directly compared initial treatment with surgery against initial treatment with chemotherapy. Some studies assessed chemotherapy without a comparator. Included studies used the following treatments for first-line chemotherapy: 5-fluorouracil (5-FU) with or without irinotecan, oxaliplatin and leucovorin; radiotherapy; and oxaliplatin-based or irinotecan-based chemotherapy. Patients differed in terms of extent of liver involvement, the presence of extra-hepatic metastatic disease and the rate of left-sided tumours. Where reported, the median follow-up of patients initially treated with chemotherapy ranged from 18 to 26 months and ranged from 23 to 30 months in patients who underwent surgery.

Two reviewers independently screened relevant studies for inclusion. Disagreements were resolved by discussion.

Assessment of study quality
The quality of the included studies was assessed using the Downs et al checklist, including criteria on study quality, external validity (generalisability of the results), study bias, confounding and selection bias, and study power. A score of 32 represented the highest quality.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Two reviewers independently extracted data on the rate of primary tumour-related complications in patients not undergoing surgery, complications of patients undergoing surgery of the primary tumour or patients receiving systemic chemotherapy, overall survival, and rate of curative surgery after treatment with systemic chemotherapy to calculate percentages and their 95% confidence intervals (CIs). The authors did not state how discrepancies were resolved.

Methods of synthesis
Percentages for each outcome were pooled along with their 95% CIs using the DerSimonian and Laird random-effects model.
Results of the review
Seven studies (n=850; 536 underwent surgery and 314 underwent chemotherapy) were included in the review: four retrospective case series; two prospective case series; and one retrospective case-control study. Sample sizes ranged from 21 to 362 patients. Study quality ranged from 12 to 21.

The pooled proportion of patients who developed bowel obstruction after receiving initial treatment with chemotherapy was 13.9 per cent (95% CI: 9.6% to 18.8%; six studies). The pooled proportion of patients experiencing haemorrhage from the primary tumour was 3.0 per cent (95% CI: 0.95% to 6.0%; four studies). One of two studies reported the development of peritonitis or fistulae in 6.1 per cent of patients due to un-resected tumour.

The pooled proportion of patients developing major complications (obstruction, haemorrhage and sepsis) after surgery was 11.8 per cent (95% CI: 4.4% to 22.0%; four studies).

Two of six studies reported statistically significant differences in survival, with patients receiving chemotherapy reporting shorter median survival rates (8.2 and 9.0 months) compared with patients treated with surgery (14 and 16 months).

Authors' conclusions
Resection of the primary colorectal tumour provided minimal palliative benefit for patients with stage IV incurable colorectal cancer, can result in major morbidity and mortality, and can potentially delay systemic chemotherapy.

CRD commentary
The review question was clear and was supported by appropriate inclusion criteria for patients, intervention, comparator and outcomes. The literature search was somewhat limited (two electronic database and one other appropriate source). The search was restricted by language, so language bias may have been introduced. There was no apparent search for unpublished studies and so potentially relevant studies may have been missed. The review process was reported for study selection and data extraction, thus reducing the potential for reviewer error and bias; the same cannot be said for validity assessment. The authors used a previously published checklist to assess validity, but the quality of the studies did not appear to be very high. Limited details were provided on treatment schedules, there was evidence of clinical heterogeneity and there was no mention of the assessment of statistical heterogeneity, which meant that it was unclear whether the synthesis was appropriate. Comparison of the two treatments was difficult as outcomes after chemotherapy were pooled separately, but were pooled as an overall percentage for treatment with surgery. Furthermore, the included studies were not particularly robust in terms of study design. Given the above limitations, it was difficult to compare the effectiveness of the two treatments from the data presented and it is, therefore, difficult to determine the reliability of the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors stated that patients should be treated with initial chemotherapy, with resection of the primary tumour restricted to the small proportion of patients who may develop complications due to the presence of primary tumour. When initial chemotherapy is started and incurable stage IV colorectal cancer becomes potentially curative, consideration should be given to combined resection of both the primary tumour and its metastases.

Research: The authors did not state any implications for research.

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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.