Treatment of gastric cancer with peritoneal carcinomatosis by cytoreductive surgery and HIPEC: a systematic review of survival, mortality, and morbidity

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CRD summary
This review concluded that cytoreductive surgery combined with heated intraperitoneal chemotherapy may improve survival in select patients with gastric cancer and peritoneal carcinomatosis. Median survival increased to 15 months where complete cytoreduction could be achieved; compared to three months with only basic supportive therapy. Limitations in the review mean that the reported values may not be reliable.

Authors' objectives
To systematically review the literature regarding the effectiveness of cytoreductive surgery combined with heated intraperitoneal chemotherapy in patients with gastric cancer who also had peritoneal carcinomatosis.

Searching
MEDLINE, EMBASE, Scopus, BIOSIS Previews and The Cochrane Library were searched for published articles in English from 2000 to 2010. Search terms were available. Further relevant studies were identified from bibliographies of included articles.

Study selection
Case series (more than five cases), randomised controlled trials (RCTs), non-randomised trials and prospective cohort studies that included adults (over 18 years old) with gastric cancer and peritoneal carcinomatosis were eligible for inclusion in the review. Studies had to evaluate cytoreductive surgery combined with heated intraperitoneal chemotherapy. Outcomes of interest were survival, mortality, morbidity, length of hospital/intensive care unit stay and quality of life.

The average age of participants in the included studies was 48.5 years (range 48 to 55). Median length of follow-up was 46 months (range 19 to 74 months). Both open and closed heated intraperitoneal chemotherapy techniques were used; the most commonly used agents were cisplatin and mitomycin. Intra-abdominal temperatures were typically between 40 and 44°C; duration of heated intraperitoneal chemotherapy ranged from 30 to 120 minutes.

Two reviewers independently selected studies for inclusion, disagreements were resolved by re-evaluation where necessary.

Assessment of study quality
The authors did not appear to formally assess study quality, but some aspects of study design were independently extracted by two reviewers.

Data extraction
Two reviewers independently extracted data on key study characteristics and outcomes from the included studies.

Methods of synthesis
Studies were primarily combined in a narrative synthesis. For survival outcomes, the median and range of average values across studies (where available) were reported. The number of treatment-related deaths and morbidities were summed across studies and divided by the number of patients to obtain an overall rate.

Results of the review
Ten studies (441 treated patients) were included in the review: one non-randomised prospective controlled trial, six prospective case series and three retrospective case series.

Overall median survival was 7.9 months (range 6.1 to 11.5; five studies). For patients with completeness of cytoreduction scores of 0 or 1, this was 15 months (range 9.5 to 43.4; four studies). One-year survival was 43% (range
22% to 68%; seven studies). Five-year survival was 13% (two studies). Treatment-related deaths was 4.8% (19/467 patients; nine studies). Overall morbidity was 21.5% (eight studies; absolute event numbers not reported).

**Authors' conclusions**

Cytoreductive surgery combined with heated intraperitoneal chemotherapy may improve survival in select patients with gastric cancer with peritoneal carcinomatosis. Median survival increased to 15 months in patients where complete cytoreduction could be achieved, compared to three months with only basic supportive therapy.

**CRD commentary**

This review was based on a clearly defined question and a wide-ranging search for relevant publications. Efforts were made to minimise potential errors and bias in data selection and extraction from the identified publications. Data from unpublished or non-English language sources were excluded. The methodological quality of the included studies was not assessed.

It appeared that the median estimates of survival were derived from the average values reported by only a subset of the included studies, which was unlikely to result in an accurate estimate of the mean survival across all included patients.

It was unclear where the value for basic supported therapy was derived; the results of the one included controlled study were not fully presented. These limitations mean that the findings of this review may not be reliable.

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

**Practice:** The authors stated that cytoreductive surgery and heated intraperitoneal chemotherapy for gastric cancer and peritoneal carcinomatosis should be considered in select patients only where the surgeon was very confident that completeness of cytoreduction (score 0) was possible.

**Research:** The authors stated that phase III prospective RCTs were needed to delineate the role of cytoreductive surgery and heated intraperitoneal chemotherapy treatment strategy for patients with gastric cancer and peritoneal carcinomatosis.

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