Does rectal cancer shrinkage induced by preoperative radio(chemo)therapy increase the likelihood of anterior resection: a systematic review of randomised trials

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CRD summary
This review assessed whether tumour shrinkage consequent on pre-operative radiotherapy, with or without chemotherapy, increases the rate of anterior resection (AR) in patients with rectal cancer. The authors concluded that the evidence of randomised trials does not suggest a beneficial effect of pre-operative radiotherapy on the rate of AR, and hence sphincter preservation. This conclusion accurately reflects the evidence of the review, but some of the evidence may not have been relevant to the review question.

Authors' objectives
To determine the impact of tumour shrinkage following pre-operative radiotherapy, with or without chemotherapy, on the rate of anterior resection (AR).

Searching
PubMed and the Cochrane Library were searched through August 2005 without any language restrictions; the search terms were reported. Abstracts from ASTRO, ESTRO and ASCO meetings between 2002 and 2005 were handsearched, as were the references of original studies, review articles and relevant books.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion. Eligible studies enrolled patients with resectable rectal carcinoma and used an intervention of pre-operative radiotherapy, with or without chemotherapy, prior to surgery, where AR was the method employed for sphincter preservation. It was not clear for all included studies at which point of treatment the decisions on type of surgery were made. The included studies used a range of different radiation schedules and (where used) number of cycles of chemotherapy, and intervals to surgery. A longer interval to surgery was the difference between the intervention and control groups in one trial. The intervention group was required to have smaller pre-operative primary tumours than the control group. The primary outcome was achievement of AR at surgery, consequently sphincter preservation was required to be reported or to be capable of being inferred from the reported data.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The validity of the studies was assessed using criteria that included allocation concealment and management of withdrawals and drop-outs. Scores attached to individual criteria were summed and expressed as a percentage of the theoretical maximum score.

Two reviewers independently assessed the studies and any disagreements were resolved through consensus.

Data extraction
Two reviewers independently extracted the data using a standardised form. Any differences were resolved through consensus. Where necessary, authors were contacted for additional data.

Methods of synthesis
The studies were combined in a narrative; statistical pooling was not carried out, although forest plots were presented. Statistical heterogeneity was assessed using the Q statistic. The studies were grouped according to whether sphincter preservation was a primary aim, a secondary aim, or not an aim. Subgroup analyses of individual studies, based on whether patients were considered necessary or probable candidates for abdominoperineal resection before radiotherapy, were reported.
Results of the review
Ten RCTs (n=4,596) were included in the review. The validity scores ranged from 0 to 100%, with six of the nine studies assessed scoring at least 80%.

There was no statistically significant difference between groups in the rate of AR in any of the included studies. Differences ranged from 19% in favour of radiotherapy to 12% in favour of the control.

Three trials presented data on the subgroups of patients considered necessary or probable candidates for abdominoperineal resection before radiotherapy. One study demonstrated a 20% benefit of radiotherapy in this subgroup (p=0.004), but had a number of methodological problems. The other two trials found no significant difference between the groups for this subgroup of patients (p>0.05 in both instances).

Authors’ conclusions
The evidence of randomised trials does not suggest a beneficial effect of pre-operative radiotherapy on the rate of AR. However, in a number of studies it is possible that surgery type was determined before radiotherapy, rendering these data irrelevant to the review question.

CRD commentary
The review question and the inclusion criteria were clear. The authors searched two relevant databases and a range of additional sources. They reported using methods designed to reduce bias and error in the assessment of validity and extraction of data, but not in the selection of studies for the review. The validity assessment used appropriate criteria but only a total score was reported, which is not the most informative procedure. The use of a narrative synthesis with accompanying forest plots, but no statistical pooling, was perhaps surprising: while procedures for evaluating statistical heterogeneity were described, their implementation was not reported. It appears that clinical heterogeneity was responsible for this approach to the synthesis. The authors’ conclusions accurately reflect the evidence of the review, but it is possible that surgery type was determined before radiotherapy in a number of studies, rendering these data irrelevant to the review question.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies investigating high-dose pre-operative radiation combined with selective brachytherapy or selective local excision for radiosensitive tumours should be conducted.

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