A meta-analysis of surgery versus conventional radiotherapy for the treatment of metastatic spinal epidural disease

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CRD summary
This meta-analysis found that, compared with conventional radiotherapy, surgery improved ability to walk for people with metastatic cancer in the spine. The authors concluded that surgery should be the primary treatment, with radiation as adjuvant therapy. The comparison between radiotherapy and surgery was indirect and based on uncontrolled observational studies; hence, the conclusions should be treated with caution.

Authors' objectives
To compare the effect of surgery versus conventional radiotherapy on the ambulatory status of people with metastatic spinal epidural disease.

Searching
PubMed was searched for articles published in the English language between 1980 and August 2003; the search terms were reported. In addition, the authors handsearched journals and examined the reference lists of review papers.

Study selection
Study designs of evaluations included in the review
Retrospective or prospective cohort studies were eligible for inclusion.

Specific interventions included in the review
Studies of radiotherapy or surgery were eligible for inclusion. Surgery involved decompression of the spinal cord circumferentially, followed by reconstruction and stabilisation, with radiation given either pre-operatively, post-operatively, or not at all. Studies of radiotherapy had to report the cumulative radiation dose and schedule. Most of the included studies involved standard external beam radiation therapy (usually 2,800 to 3,200 cGy total dose divided over 7 to 12 days).

Participants included in the review
Eligible studies included adults with symptomatic metastatic spinal disease. In several of the surgery studies, the participants had previously received radiotherapy. The average age was 56 years for surgery patients and 63 years for radiotherapy. Forty-eight per cent of the surgery patients and 51% of the radiotherapy patients were women. Two thirds had metastatic lesions located primarily in the thoracic spine (68% in both the surgery and radiotherapy studies). The primary cancer sites were predominantly breast, renal, lung, and prostate. Two per cent of participants had primary spinal bone tumours other than metastatic disease; these did not conform to the inclusion criteria but could not be separated in the data analysis.

Outcomes assessed in the review
To be eligible for inclusion, the studies had to report on ambulatory status before and after treatment and to include data on age, gender, site of primary disease and site of disease within the spine. The primary outcome of the review was ambulation: success or rescue, defined as the proportion of people ambulatory after treatment and the proportion regaining ambulatory function, respectively. Participants were considered ambulatory if they could walk with or without assistance. Secondary outcomes (pain, sphincter function, survival, complications and local recurrence) were also assessed.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review. Two authors reviewed articles, but it was unclear whether the assessment was independent or how any disagreements were resolved.
Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two authors extracted the data. The data extraction categories were reported. For each study, the authors used data on ambulatory function before and after intervention to calculate effect sizes and 95% confidence intervals for ambulatory success and rescue.

Methods of synthesis
How were the studies combined?
For ambulatory success and rescue, the studies were combined by meta-analysis using a ‘mixed effects’ model because of the suspected presence of both explained and unexplained heterogeneity. Studies with small sample sizes and high or low effect sizes had more conservative effect sizes assigned for use within the model (‘Windsorising’, see Other Publications of Related Interest no.1). A pooled effect size for radiation and surgery combined was calculated. Crude risk ratios (RRs) were calculated to compare the effectiveness of radiation and surgery.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q statistic. The authors investigated sources of heterogeneity using univariate and multivariate meta-regression.

Results of the review
The review included 28 studies: 24 focused on surgery (999 participants) and 4 focused on radiation (543 participants). Apart from one prospective cohort study with internal controls, all studies were uncontrolled, non-randomised prospective or retrospective cohort studies.

Ambulatory success.
People receiving surgery were 1.3 times more likely to be ambulatory after treatment: 85% surgery versus 64% radiotherapy (crude RR 1.28, 95% CI: 1.20, 1.37, P<0.001). Significant heterogeneity was present in the meta-analysis for this outcome (Q=164.6, P<0.001). Age, gender, primary pathology and lesion distribution did not statistically significantly influence these findings.

Ambulatory rescue.
People receiving surgery were twice as likely to regain ambulatory function compared with those undergoing radiotherapy (crude RR 1.99, 95% CI: 1.63, 2.44, P<0.001), but there was significant heterogeneity (Q=480.9, P<0.001) which, when controlled for, meant that the differences between treatments were not statistically significant.

The authors also reported on secondary outcomes including pain, survival, complications and local recurrences, though not all studies included information about these outcomes.

Authors’ conclusions
Compared with radiotherapy, surgery is associated with improved ambulatory success and rescue for people with metastatic spinal epidural disease. For people with newly diagnosed disease, surgery should usually be the primary treatment, with radiation as adjuvant therapy.

CRD commentary
This meta-analysis included a defined research question and inclusion and exclusion criteria. Only one database was searched and studies in languages other than English were excluded. This reduces certainty that all relevant studies were identified. Unpublished material was not sought and publication bias was not assessed, so there is a possible risk of
publication bias affecting the review. The authors did not report on any methods used to assess the validity of the included studies, which makes it difficult to assess the validity of the review or the studies on which it was based. However, to help readers assess generalisability, detailed information on study characteristics was tabulated and described. A significant number of participants in the ‘surgery’ group had received prior radiotherapy treatment; the impact of this is uncertain.

The authors reported their analysis method and rationale in detail. They acknowledged and attempted to investigate differences between the studies. However, heterogeneity was significant and it is unclear whether pooling such a diverse group of studies could produce a meaningful result. It is also uncertain whether the ‘recoding’ of some figures for use in the model had any impact, and the authors did not comment on the potential impact on the findings. All the included studies were non-randomised and uncontrolled, and the comparison between surgery and radiotherapy was indirect. The data presented support the authors’ conclusions but, in view of the above limitations, the findings should be treated with caution.

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

Practice: The authors stated that surgery should usually be the primary treatment for metastatic spinal epidural disease, with radiation as adjuvant therapy.

Research: The authors stated that future research should examine the effects of new interventions such as minimally invasive spine surgery and stereotactic radiosurgery on a multicentre basis, with quality of life and ambulatory status quantified using known mobility measures. They suggested that a trial comparing the effects of stereotactic radiotherapy versus surgery would be useful.

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