Effectiveness of reirradiation for painful bone metastases: a systematic review and meta-analysis

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CRD summary
The review concluded that re-irradiation of painful bone secondary cancers was effective for pain relief in just over half of the patients treated, although approximately 40% of patients did not benefit. The suboptimal quality of the evidence base, and the potential for biases, in the included studies and in the review, limits the reliability of the authors’ conclusions.

Authors' objectives
To determine the effectiveness of re-irradiation for achieving pain control in patients with painful bone metastases.

Searching
The Cochrane Library, EMBASE and MEDLINE were searched from 1980 up to January 2011 for articles in English, German, French and Dutch. Search terms were reported. Cross referencing of systematic reviews, papers, editorials and textbooks was undertaken. Unpublished studies were not sought.

Study selection
Studies of re-irradiation for achieving pain control in patients with painful bone metastases who were not sufficiently responding to initial radiotherapy or exhibiting recurrent pain after initial response were eligible for inclusion. To be included, the initial treatment and the re-treatment had to be external beam radiotherapy, and re-treatment had to be in the same lesion. The primary outcome was pain response rate. For inclusion in the meta-analysis, studies had to include at least ten patients and outcomes had to be available on an individual patient basis.

Patients in the included studies had irradiated tumours of the pelvis (38%), spine (36%), proximal long bones (12%) and other locations (14%). The initial radiotherapy ranged from 4 to 24GY. Included studies were published from 1988 to 2004.

The authors did not state how many reviewers undertook study selection.

Assessment of study quality
Two reviewers independently performed quality assessment using the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) framework. Quality items appraised were: standardisation of re-irradiation, patient based questionnaire, standardised pain scale, moment of response assessment standardised, follow-up of more than 80%, and study objectives included in re-treatment outcome.

Data extraction
Data were extracted on pain response rates and used to calculate partial responses, complete response and overall responses, with 95% confidence intervals. Data on toxicity were also extracted. Study authors were contacted for missing data.

Two reviewers independently extracted the data.

Methods of synthesis
Random-effects meta-analysis was used to calculate pooled overall response rates and 95% confidence intervals. $I^2$ was used to assess statistical heterogeneity. Sensitivity analysis was deemed infeasible.

A narrative synthesis was also presented.

Results of the review
Ten studies were included in the review (613 patients re-irradiated); seven studies were included in the meta-analysis.
(527 re-irradiated patients). The study sample size of re-irradiated patients ranged from four to 173 patients. Study types included two randomised controlled trials (RCT), four parallel group studies, two prospective cohort studies and two retrospective series studies. The quality of the included studies was variable; most studies used a standardised pain scale, but few standardised the moment of response assessment.

The pooled overall response rate for re-irradiated patients was 58% (95% CI 49% to 67%; $I^2=63%$; seven studies). The complete response rates for irradiation ranged from 16 to 28%. The partial response rates ranged from 28 to 45%. The proportion of patients experiencing toxicity with re-irradiation ranged from 0 to 31% in three studies.

**Authors' conclusions**

Re-irradiation of painful bone metastases was effective for pain relief in just over half of the patients treated, although approximately 40% of patients did not benefit.

**CRD commentary**

Inclusion criteria for the review were defined. Several relevant data sources were searched. Attempts were made to reduce reviewer error and bias during data extraction and quality assessment, but it was not clear if the same attempts were made for study selection.

Quality assessment was undertaken according to specific quality factors, which indicated that the reliability of the evidence base was sub-optimal (most of the studies were observational). A narrative synthesis was presented for most outcomes. Meta-analysis was used to pool overall response rate data, although the analysis may have not been appropriate as observational and RCT data were pooled together. The analysis also had a high level of statistical heterogeneity, which indicated that the data may not have been suitable for pooling. The authors noted that the reasons for re-irradiation were not always specified, which may have introduced selection bias. The authors also noted that the timing of irradiation was not standardised in any of the studies, which may have biased the results.

The suboptimal quality of the evidence base, and the potential for biases in the included studies and in the review, limits the reliability of the authors' conclusions.

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

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that more research was needed to provide optimal palliative care. The authors also noted that the results of consensus guidelines applied to the S20 study were eagerly awaited.

**Funding**

Not stated.

**Bibliographic details**


PubMedID
22300568

DOI
10.1016/j.ijrobp.2011.10.080

Original Paper URL
http://www.redjournal.org/article/S0360-3016(11)03488-2/abstract

Indexing Status
Subject indexing assigned by NLM
MeSH
Bone Neoplasms /radiotherapy /secondary; Female; Humans; Male; Pain /etiology /radiotherapy; Palliative Care /methods; Retreatment /adverse effects /methods; Treatment Outcome

AccessionNumber
12012042531

Date bibliographic record published
26/11/2012

Date abstract record published
13/03/2013

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.