Journal Watch


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Abstract

**Background:** Recent randomized studies reported that single fraction radiotherapy was as effective as multifraction radiotherapy in relieving pain due to bone metastasis. However, there are concerns about the higher re-treatment rates and the efficacy of preventing future complications such as pathological fracture and spinal cord compression by single fraction radiotherapy.

**Objectives:** To undertake a systematic review and meta-analysis of single fraction radiotherapy versus multi-fraction radiotherapy for metastatic bone pain relief and prevention of bone complications.

**Search strategy:** Trials were identified through MEDLINE, EMBASE, Cancerlit, reference lists of relevant articles and conference proceedings. Relevant data was extracted.

**Selection criteria:** Randomized studies comparing single fraction radiotherapy with multi-fraction radiotherapy on metastatic bone pain.

**Data collection and analysis:** The analyses were performed using intention-to-treat principle. The results were pooled using meta-analysis to estimate the effect of treatment of pain response, re-treatment rate, pathological fracture rate and spinal cord compression rate.

**Main results:** Eleven trials that involved 3435 patients were identified. Of 3435 patients, 52 patients were randomized more than once for different painful bone metastasis sites. Altogether, 3487 painful sites were randomized. The trials included patients with painful bone metastases of any primary sites, but were mainly prostate, breast and lung. The overall pain response rates for single fraction radiotherapy and multi-fraction radiotherapy were 60% (1059/1779) and 59% (1038/1769) respectively, giving an odds ratio of 1.03 (95% confidence interval [CI], 0.89-1.19) indicating no difference between the two radiotherapy schedules. There was also no difference in complete pain response rates for single fraction radiotherapy (34% [497/1441]) and multi-fraction radiotherapy (32% [463/1435]) with an odds ratio of 1.11 (95% CI 0.94-1.30). Patients treated by single fraction radiotherapy had a higher re-treatment rate with 21.5% (267/1240) requiring re-treatment compared to 7.4% (91/1236) of patients in the multi-fraction radiotherapy arm (odds ratio 3.44 [95% CI 2.67-4.43]). The pathological fracture rate was also higher in single fraction radiotherapy arm patients. Three percent (37/1240) of patients treated by single fraction radiotherapy developed pathological fracture compared to 1.6% (20/1236) for those treated by multi-fraction radiotherapy (odds ratio 1.82 [95% CI 1.06-3.11]). The spinal cord compression rates were similar for both arms (odds ratio 1.41 [95% CI 0.72-2.75]). Repeated analyses excluding dropout patients gave similar results.

**Authors’ conclusions:** Single fraction radiotherapy was as effective as multi-fraction radiotherapy in relieving metastatic bone pain. However, the re-treatment rate and pathological fracture rates were higher after single fraction radiotherapy. Studies with quality of life and health economic end points are warranted to find out the optimal treatment option.
Comments

**Strengths/Uniqueness:**
The review addressed a clear question with well-defined inclusion criteria for the interventions, comparators, participants, study design and outcomes. Eleven trials that involved 3435 patients were included. The results derived for the primary studies and pooled analysis were well reported.

**Weaknesses:**
The quality of the trials was assessed, but the results of this assessment were not reported. Lack of information on the primary studies. Differences between the methods used in the primary trials to assess pain relief might have impacted on the review’s results. The efficacy of treatment relative to no treatment was not established and the treatment difference for pathological fracture only just reached statistical significance.

**Relevance to Palliative Care:**
Single fraction radiotherapy is as effective as multi-fraction radiotherapy in relieving metastatic bone pain. Many factors will contribute to the radiation oncologist’s decision. Incorporation of different modalities (e.g. radioisotopes or bisphosphonates) may further improve the efficacy of these two treatments.