Brachytherapy for cervix cancer: low-dose rate or high-dose rate brachytherapy; a meta-analysis of clinical trials
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CRD summary
This review concluded that there were no differences between high-dose rate and low-dose rate brachytherapy for overall survival, local recurrence and late complications for clinical stages I, II and III of cervical cancer. A degree of caution might be required in interpreting these conclusions, given the limited quality of included RCTs and methodological concerns in the review methods.

Authors' objectives
To compare the efficacy and safety of high-dose rate brachytherapy with low-dose rate brachytherapy in the treatment of cervical cancer.

Searching
MEDLINE, CANCERLIT and The Cochrane Library were searched from 1996 to 2007. Search terms were reported. Physician Data Query (PDQ) clinical trials database, proceedings of the 1997 to 2007 annual meetings of American Society of Clinical Oncology and American Society for Radiation Oncology were searched for new or ongoing trials. Reference lists of retrieved publications were screened.

Study selection
Randomised controlled trials (RCTs) that compared high-dose rate brachytherapy with low-dose rate brachytherapy following pelvic radiotherapy in patients of at least 18 years old with histologically confirmed cervical cancer treated with radiotherapy alone or in combination with chemotherapy were eligible for inclusion. The review outcomes were overall mortality, local recurrence and treatment complications.

Included studies were published between 1993 and 2006. Most patients were at clinical cancer stage II or III. Low-dose rate treatment regimens varied from 25Gy to 75Gy in 1-4 fractions. High-dose rate treatment regimens varied from 15Gy to 38Gy in 2-5 fractions. The pelvic radiotherapy dose for included patients ranged from 16Gy to 50Gy.

Two reviewers independently assessed studies for inclusion. Any disagreements were resolved by a third reviewer.

Assessment of study quality
The quality of RCTs was assessed with the criteria: randomisation, allocation concealment, blinding, withdrawal, intention-to-treat analyses, sample size calculation and completeness of follow-up.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were extracted on the number of patients who experienced an event. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined in meta-analyses, using the fixed-effects model of Mantel-Haenszel. Pooled odds ratios with 95% CIs were calculated. Statistical heterogeneity was investigated using $X^2$ and $I^2$ statistics. Subgroup analyses were conducted on different clinical cancer stages. Publication bias was visualised using funnel plots.
Results of the review
Five RCTs (n=2,145) were included in meta-analyses. For methodological quality of trials, randomisation, allocation concealment and withdrawals were not adequately reported and intention-to-treat analyses were not performed. Completeness of follow-up was adequate in most trials. No trials had adequate blinding. The quality of evidence was low for outcomes of mortality and local recurrence in patients with clinical stage I and moderate for other clinical outcomes.

Compared with low-dose rate brachytherapy, high-dose rate brachytherapy had no significant difference in overall mortality (OR 0.94, 95% CI 0.78 to 1.13; five RCTs) and local recurrence (OR 1.05, 95% CI 0.85 to 1.29; five RCTs) for all clinical stages. No significant heterogeneity was observed.

No significant differences were observed in the rate of grade 3 or 4 rectal, bladder and small intestine complications between the two groups.

In subgroup analyses, there were no significant differences between high-dose rate and low-dose rate brachytherapy for overall mortality and local recurrence in patients with clinical stages I, II and III.

The authors did not report the results of assessing publication bias.

Authors' conclusions
There were no differences between high-dose rate and low-dose rate brachytherapy for overall survival, local recurrence and late complications for clinical stages I, II and III of cervical cancer.

CRD commentary
This review's inclusion criteria were clear. Several relevant databases were searched. Efforts were made to find both published and unpublished studies, which minimised potential for publication bias. The authors did not state whether language restrictions were applied in the search, which made it difficult to assess the risk of language bias. Steps were taken to minimise bias by having more than one reviewer undertake the study selection; it was unclear whether the processes of quality assessment and data extraction were also performed in duplicate. Relevant criteria were used to examine the study quality. Statistical heterogeneity was assessed and appropriate statistical methods were used to pool the results. The authors' conclusions reflected the evidence presented. However, a degree of caution might be required in interpreting these conclusions, given the generally poor quality of included RCTs and other potential methodological concerns outlined above.

Implications of the review for practice and research
Practice: The authors stated that use of high-dose rate for all clinical stages of cervix cancer should be recommended. Given some potential disadvantages of low-dose rate brachytherapy, high-dose rate brachytherapy should be considered a standard treatment strategy for patients with cervical cancer.

Research: Further trials were required to investigate three dimensional brachytherapy, fractionation and dose adjustment of the total dose in reducing complications without compromising the treatment effects.

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