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Title **Intensity-Modulated Radiotherapy for the Treatment of Prostate Cancer: A Systematic Review and Economic Evaluation**

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Aim

To evaluate the clinical and cost effectiveness of intensity-modulated radiotherapy (IMRT) for radical treatment of prostate cancer (PC).

Conclusions and results

No randomized controlled trials (RCTs) of IMRT versus 3-dimensional conformal radiotherapy (3DCRT) in PC were available, but 13 nonrandomized studies comparing IMRT with 3DCRT were found (5 were abstracts). One abstract reported overall survival. Biochemical relapse-free survival was not affected by treatment group, except where the dose differed between groups, in which case higher dose IMRT was favored over lower dose 3DCRT. Most studies reported an advantage for IMRT in GI toxicity, attributed to increased conformality of treatment compared with 3DCRT, particularly with regard to volume of rectum treated. Genitourinary toxicity was indicated to be worse for patients treated with dose escalated IMRT, but most studies did not find a significant treatment effect. Health-related quality of life (HRQoL) improved for both treatment groups following radiotherapy, with any group difference resolved by 6 months after treatment. No comparative studies of IMRT versus prostatectomy were identified. No comparative studies of IMRT in PC patients with bone metastasis were identified. The comparative data of IMRT versus 3DCRT seem to suggest that higher doses (up to 81 Gy) can improve biochemical survival in patients with localized PC, concurring with data on CRT. The data also suggest that toxicity can be reduced by increasing conformality of treatment, particularly as regards GI toxicity, which can be more easily achieved with IMRT than 3DCRT. Whether differences in GI toxicity between IMRT and 3DCRT are sufficient for IMRT to be cost-effective is uncertain, depending on the difference in incidence of GI toxicity, its duration, and the cost difference between IMRT and 3DCRT.

Recommendations

Clinical advice suggests that most radiotherapy (RT) centers already possess the equipment required to deliver IMRT, but that lack of available staff hinders implementation. 3DCRT may be safely delivered at the currently recommended total dose of 74 Gy, and there is no evidence that PSA survival is improved by giving IMRT at the same dose as 3DCRT. There is evidence that IMRT reduces toxicity, in particular late GI toxicity. The magnitude of the difference is uncertain, which, together with uncertainties in other variables makes the cost effectiveness of IMRT in comparison to 3DCRT uncertain. Assuming a difference in late GI toxicity of 15%, the probability of IMRT being more cost effective than 3DCRT is only true for a MAICER of ≥30 000 pounds sterling (GBP).

Methods

A systematic literature review of the clinical and cost effectiveness of IMRT in PC was conducted. Comparators were 3DCRT or radical prostatectomy. Outcomes sought were overall survival, biochemical relapse-free survival, toxicity, and HRQoL. We searched 15 electronic bibliographic databases (eg, MEDLINE, EMBASE, CINAHL, MEDLINE In-Process & Other Non-Indexed Citations) in January 2009 and updated in May 2009. Reference lists of relevant articles were checked. Only studies in English were included. An economic model was developed to examine the cost effectiveness of IMRT in comparison to 3DCRT. Four scenarios were modeled based on the studies, which reported both prostate-specific antigen (PSA)survival and late gastrointestinal (GI) toxicity. In two scenarios equal PSA survival was assumed for IMRT and 3DCRT, the other two having greater PSA survival for the IMRT cohort. As data on clinical outcomes were limited, the model estimates progression to clinical failure and PC death from the surrogate outcome of PSA failure.

Further research/reviews required

See Executive Summary link www.hta.ac.uk/project/1788.asp.

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