Radiotherapy is a cost-effective palliative treatment for patients with bone metastasis from prostate cancer

Konski A

Health technology
Several palliative treatments for patients with bone metastasis from prostate cancer were examined. These were pain medication only (best supportive care, BSC), chemotherapy consisting of mitoxantrone and prednisone, and single and multiple fractions (SFX and MFX, respectively) of external beam radiotherapy (EBRT). BSC consisted of 120 mg/day OxyContin for a total dose of 3,600 mg/month. Chemotherapy was supplied as a 12.5-mL vial of mitoxantrone.

Type of intervention
Palliative care.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of men with hormone-refractory prostate cancer who had developed a painful solitary bone metastasis.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
Some clinical data came from studies published from 1986 to 2003. No dates for resource use were explicitly reported. The price year was not reported.

Source of effectiveness data
The effectiveness data was derived from a synthesis of completed studies and author's opinions.

Modelling
Different Markov models were used to examine the costs and survival associated with the four palliative treatments under evaluation. Monthly cycles were used. The time horizon of the models was 24 months.

The models for SFX- and MFX-EBRT were the same except for the initial cost of the treatment. On entering the model at either SFX- or MFX-EBRT, patients could either die or be alive. If the patients were alive, they either had pain relief or had pain and underwent re-treatment with the same fractionation schedule.

Patients started treatment with chemotherapy and could either die or be alive. If alive, they could remain pain-free or develop pain. If they developed pain, they received MFX-EBRT. If they remained pain free they proceeded through six
cycles of chemotherapy according to the protocol. Symptomatic patients received MFX-EBRT.

With BSC, patients entered the model and could either die or be alive. If the patients were alive, they stayed in the state for 1 month and then once again could either die or be alive. Beta-distributions were associated to monthly transition probabilities and second-order Monte Carlo simulations were performed.

**Outcomes assessed in the review**
The outcomes assessed from the literature for MFX- and SFX-EBRT were:

- the survival rate at 2 years,
- the probability of pain,
- the re-treatment rate, and
- utility values.

The survival rate and rate of pain relief associated with chemotherapy were also assessed.

**Study designs and other criteria for inclusion in the review**
The author stated that a review of the literature was undertaken to identify the primary studies. No details of the review were reported.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
Nine primary studies provided clinical evidence.

**Methods of combining primary studies**
A narrative approach appears to have been used to combine the primary estimates.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The overall survival rate with both MFX-EBRT and SFX-EBRT at 2 years was 20%.

The probability of pain at 1 year ranged from 47 to 50% for the SFX group and from 40 to 50% for the MFX group.

The re-treatment rate was 10 to 11% for the MFX group and 22 to 23% for the SFX group.
The utility values were 0.60 for MFX and SFX.

The survival rate associated with chemotherapy was 20% at 2 years.

The rate of pain relief was 40% at 1 year.

**Methods used to derive estimates of effectiveness**
The author made some assumptions to derive clinical estimates of effectiveness that were not found in the literature.

**Estimates of effectiveness and key assumptions**
In the radiotherapy branch, the utility for the re-treatment state was 0.5 and the utility for patients receiving pain medication after re-treatment failed was 0.2. The utility for months spent during chemotherapy was 0.6. The probability of success for pain medication was equal to the pain medication portion of this analysis. A utility of 0.4 was estimated for the first 6 months of BSC, and this decreased by 0.05 every 2 months. The overall survival at 2 years with BSC was 20%.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the quality-adjusted life-months (QALMs). These were estimated by combining survival and quality of life data using the decision model. Given the short time horizon of the model, no discounting was applied.

**Direct costs**
The cost analysis was performed from the perspective of the third-party payer (e.g. Medicare). The health services included in the economic evaluation were radiotherapy, chemotherapy, and pain medication within the BSC protocol. A detailed breakdown of the cost items was reported. Visits to the doctor and other health care professionals were not included because they were assumed to have been comparable across treatments. The unit costs and the quantities of resources used were reported separately for most items. The costs were derived from Medicare reimbursement rates, average wholesale prices and experts' opinions. Resource use was estimated on the basis of usual and reasonable consumptions of resources for the treatment of bone metastases, although the source of the data was unclear. Discounting was not relevant since the costs were incurred during a 2-year time horizon. The price year was not stated.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case, but stochastic distributions were assigned in the sensitivity analysis (see 'Sensitivity Analysis' section below).

**Indirect Costs**
The indirect costs were not considered in the economic evaluation.

**Currency**
US dollars ($).

**Sensitivity analysis**
A probabilistic sensitivity analysis was performed using a second-order Monte Carlo simulation to define confidence intervals for the estimated cost-utility ratios. One- and two-way sensitivity analyses were also carried out on the cost and utility values. The author appears to have set the ranges of values used.
Estimated benefits used in the economic analysis
The estimated QALMs were 5.75 with BSC, 6.1 with SFX-EBRT, 6.25 with MFX-EBRT and 4.93 with chemotherapy. The incremental effectiveness over BSC was 0.35 with SFX-EBRT, 0.5 with MFX-EBRT and -0.82 with chemotherapy.

Cost results
The estimated costs were $11,700 with BSC, $11,900 with SFX-EBRT, $13,200 with MFX-EBRT and $15,300 with chemotherapy. The incremental costs in comparison with BSC were $200 with SFX-EBRT, $1,500 with MFX-EBRT and $3,600 with chemotherapy.

Synthesis of costs and benefits
An incremental cost-utility ratio was calculated to combine the costs and benefits of the alternative palliative strategies.

The incremental analysis showed that the cost per quality-adjusted life-year (QALY) gained in comparison with BSC was $6,857 with SFX-EBRT and $36,000 with MFX-EBRT. Chemotherapy was dominated by BSC, which was both more effective and less expensive.

The probabilistic sensitivity analysis showed that the majority of cost-utility ratios associated with SFX-EBRT over BSC fell within the commonly used threshold for cost-effectiveness (i.e. $50,000 per QALY). Also, the majority of the cost-utility ratios of MFX-EBRT versus BSC were below the threshold, although a higher percentage of points were above the threshold for the comparison between SFX-EBRT and BSC. The cost-effectiveness of SFX-EBRT did not change when alternative assumptions about the costs and utilities associated with chemotherapy were used. However, when all utility values were assumed to have been 1 (thus eliminating any bias against treatment that could be more toxic), all treatments were basically similar in terms of their effectiveness, highlighting the need for utility-adjustment in the evaluation of palliative treatments.

Authors' conclusions
Single-fraction external beam radiotherapy (SFX-EBRT) was the most cost-effective treatment for patients with bone metastasis from prostate cancer in the USA. The results of the model were quite robust to variations in most inputs.

CRD COMMENTARY - Selection of comparators
The author stated that the treatments evaluated in the study represented available palliative care options for patients with bone metastasis from prostate cancer. Dosages and treatment protocols were reported. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from the literature. However, the methods and conduct of the review were not reported. No information on the search and inclusion or exclusion criteria was provided. The number of studies included in the review was reported, but the primary studies were not described. Thus, it was not possible to assess the validity of the primary studies. The methods used to extract and then combine the primary estimates were not reported. The author noted that some of the data used in the decision model were not specific to prostate cancer. Some assumptions were also made to derive clinical data that were not available from the literature, and most of these assumptions were varied in the sensitivity analysis.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate as it reflected the impact of the interventions on both expected survival and quality of life. The utility weights came from the literature and from author's opinions. However, there was limited information on the primary sources of the utility values. The use of QALYs has the further advantage of making the benefits estimated in the current study comparable with the benefits of other health care
interventions. The use of different utility values had a strong impact on the final cost-utility ratios.

Validity of estimate of costs
The costs included were consistent with the perspective adopted in the study, although they were restricted to direct medical costs. A detailed breakdown of the cost items was provided and some information on the quantities of resources used was given. A justification was provided for the exclusion of some costs. The unit costs were reported for most items. No statistical analysis of the costs was performed in the base-case, but the impact of variations in key cost data was investigated in the sensitivity analysis. Further, probabilistic distributions were assigned to all cost estimates in the Monte Carlo simulation. The source of the costs was given. Discounting was not relevant and was not applied. The price year was not given, which limits the possibility of performing reflation exercises in other time periods. The author noted some difficulties in using precise estimates of the costs.

Other issues
The author did not make extensive comparisons of the findings with those from other studies. The issue of the generalisability of the study results to other setting was also not addressed. However, several sensitivity analyses were performed, which partially enhance the external validity of the study. A justification for the choice of the decision model was provided, although a graphical representation of the model was not presented. Similarly, health states and transition probabilities were presented in a narrative way. The study referred to patients with bone metastasis from prostate cancer and this was reflected in the author's conclusions.

Implications of the study
The study results support the use of SFX-EBRT for the palliative care of patients with bone metastasis from prostate cancer.

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None stated.

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Other publications of related interest

