Cost-effectiveness of surgery plus radiotherapy versus radiotherapy alone for metastatic epidural spinal cord compression


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Two treatments for metastatic epidural spinal cord compression (MESCC) were examined, surgery in addition to radiotherapy (S+RT) versus radiotherapy alone (RT). RT was administered at a dose of 30 Gy at 3 Gy/fraction per day inclusive of one vertebral body above and below the visible lesion. Surgery was performed with the intention of removing as much tumour as possible, providing immediate decompression, and stabilising the spine.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with MESCC. The metastatic tumour types excluded were lymphomas, myelomas, leukemias and germ cell tumours. Patients were required to have no history of RT to the site and an expected survival of 12 weeks.

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

Dates to which data relate
The effectiveness data came from a study published in 2005. No dates for resource use were reported. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on a different sample of patients from that used in the effectiveness analysis.

Study sample
Power calculations, if performed, were not reported. Of 123 patients initially assessed for eligibility, 101 patients were finally included. There were 50 patients in the S+RT group and 51 patients in the RT group. The mean age of the sample was 59.76 years (age range: 25 to 84). The proportion of women was 30.9%. Of the 22 patients considered to be ineligible, 9 individuals failed to meet the inclusion criteria of the primary trial, 5 refused to participate, and 8 were
excluded because of physician refusal.

**Study design**
This was a multi-centred, randomised clinical trial. Randomisation was stratified by treating institution, tumour type, ambulatory status, and relative stability of the spine. The number and types of medical institutions involved were not described. Surgery was performed within 24 hours of study entry. RT started within 2 weeks of surgery in the S+RT group and within 24 hours of study entry in the RT group. The patients were followed until death. No patients were lost to follow-up. However, 10 patients (7 in the S+RT group and 3 in the RT group) were censored when the trial ended prematurely because an interim analysis showed that S+RT was more effective. Blinding was not performed.

**Analysis of effectiveness**
The analysis of effectiveness appears to have been conducted on an intention to treat basis since all patients included in the initial study sample were taken into account. The primary outcome measure was the ability to walk after treatment (days of ambulation). A secondary measure was survival. A Weibull regression was used to deal with censoring of 10% of the sample. Thus, both survival and ambulatory data were extrapolated to the end of follow-up for the entire cohort of patients in the trial, producing mean survival and ambulation. Mean expected outcomes generated by the Weibull regression were reported together with actual data observed in the clinical trial. The baseline comparability of the study groups was not demonstrated, but the study design and methods of randomisation are likely to have ensured that there were no statistically significant differences between the two groups.

**Effectiveness results**
The proportion of patients able to ambulate changed from 69% to 57% in the RT alone group and from 68% to 84% in the S+RT group.

The observed mean days of ambulation were 91.25 in the RT alone group and 289.64 in the S+RT group.

The observed mean days of survival were 216.86 in the RT alone group and 351.96 in the S+RT group.

The Weibull analysis showed that the mean expected days of survival were 221.11 in the RT alone group and 377.06 in the S+RT group. The mean expected days of ambulation were 92.34 in the RT alone group and 312.47 in the S+RT group.

**Clinical conclusions**
The effectiveness analysis showed that S+RT was more effective than RT alone, both in terms of ability to walk after treatment and in terms of survival.

**Measure of benefits used in the economic analysis**
The summary benefit measures used in the cost-effectiveness analysis were ambulation ability and survival. These were derived from the effectiveness analysis using a Weibull approach.

**Direct costs**
The perspective of the analysis was societal, thus both the medical and non-medical direct costs were considered. In particular, the analysis included diagnostic tests, treatment planning, surgery, RT, hospital stay, personnel, medications, institutionalisation and in-home nursing care. The impact of complications associated with RT was considered. The unit costs were not presented separately from the resource quantities, most costs being presented as macro-categories. Resource use was not derived from the clinical trial but was based on data prospectively derived from a sample of 70 patients admitted at the Vancouver Hospital and Health Sciences Center. The opinions of some experts were also used to derive the probabilities of RT-related complications. The costs came from multiple sources such as published studies, the St. Paul's Hospital Cost Model, the British Columbia Medical Association Guide to Fees, the British Columbia NHS Economic Evaluation Database (NHS EED) Produced by the Centre for Reviews and Dissemination Copyright © 2020 University of York
Pharmacare Low Cost Alternative Drug Booklet, Statistics Canada, and an Ontario regional cancer centre. Discounting was not relevant as the costs were incurred during a short timeframe. The price year was 2003.

**Statistical analysis of costs**
Probabilistic distributions were assigned to the costs. A log-normal distribution was fitted to the cost of surgery, while gamma distributions were used for days in hospital and general care wards.

**Indirect Costs**
Indirect costs (i.e. productivity losses related to disease), were not included in the economic analysis, probably due to the severity of the disease.

**Currency**
Canadian dollars (CAD). The exchange rate from CAD to US dollars ($) was CAD 1 = $0.82.

**Sensitivity analysis**
A univariate sensitivity analysis was carried out in which several economic parameters were varied in order to establish the robustness of the analysis. For example, the cost of surgery and the number of days spent in the intensive care unit or in the general ward were varied over the published confidence intervals, while hospital costs were varied by +/- 25%.
Moreover, post-intervention and pharmaceutical treatment costs were considered to be equal between treatment groups.
A probabilistic sensitivity analysis based on a Monte Carlo simulation was also performed, and the probability distributions of the cost of surgery, length of hospital stay, and total time of ambulation and survival were sampled 5,000 times. The simulation generated a cost-effectiveness acceptability curve. Finally, mean survival and ambulation were varied at the 25th and 75th percentiles in a two-way sensitivity analysis.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section for mean expected days of survival and ambulation.

**Cost results**
The total costs were not reported, but the authors stated that the additional costs of S+RT over RT alone were CAD 13,220 per patient.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios (ICERs) were calculated in order to combine the costs and benefits of the two strategies.

The incremental cost per additional day of ambulation with S+RT in comparison with RT alone was CAD 60.06. The incremental cost per additional life-year gained was CAD 30,940.16.

The probabilistic sensitivity analysis showed that S+RT was the dominant option (more effective and less expensive) in 18% of all simulations. The cost-effectiveness acceptability curve showed that 50% of the ICERs were less than CAD 57 and 95% of the ICERs were less than CAD 242 per additional day of ambulation.

The univariate sensitivity analysis suggested that the assumption of common post-hospitalisation cost had the greatest impact on the ICER, which was higher than that for the base-case (CAD 198.02 per extra ambulation day). Variations in other data did not substantially alter the results of the study.

**Authors' conclusions**
The use of surgery together with radiotherapy (RT) for the treatment of metastatic epidural spinal cord compression (MESCC) was likely to be cost-effective in comparison with RT alone in the Canadian context.

**CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparators was clear. The authors stated that RT and surgery were the most commonly used treatments for MESCC. Readers were referred to the original trial for more detail on the alternatives compared. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis of effectiveness was based on a clinical trial, which was appropriate for the study question. In practice, the use of a randomised design should limit the impact of selection bias. The length of follow-up was appropriate, although the trial was ended prematurely because of the superiority of the S+RT approach. The multi-centred design of the study enhances the representativeness of the study sample. Other details of, for example, the use of power calculations or the baseline comparability of the study groups, were not reported in this economic evaluation. The authors described the statistical approach used to estimate the clinical impact of the two treatments, taking into account the censoring of data. The authors noted that most of the centres where treatment was performed offered a relatively high level of surgical expertise, thus caution will be required if extrapolating the results of the analysis to other medical centres. It was noted that factors such as tumour type could have affected the conclusions of the analysis, although the authors pointed out that statistical analyses suggested that gender and ability to ambulate were the only predictors of survival. All these features strengthen the robustness of the analysis.

**Validity of estimate of measure of benefit**

The authors justified their choice of the primary benefit measure and stated that ambulation represents a valid measure of treatment effectiveness for patients with MESCC. However, life-years were also used as an alternative measure, and this measure would be more readily comparable with the benefits of other health care interventions. Despite the apparent impact of the intervention on quality of life, the lack of published data on utility precluded the use of quality-adjusted life-years as a summary benefit measure.

**Validity of estimate of costs**

The cost analysis was carried out from a societal perspective, but indirect costs were excluded because of the severity of the disease. The categories of costs included appear to have been appropriate since the costs incurred after discharge were considered. The authors reported all the sources from which the costs were derived, but a breakdown of the cost items was not provided. The costs were mainly presented as macro-categories or derived from published studies. This could limit the possibility of replicating the analysis in other settings. Nevertheless, the impact of varying the cost estimates was extensively addressed in the sensitivity analysis, which enhances the external validity of the cost analysis. The price year was reported and this will assist any reflation exercises in other time periods.

**Other issues**

The authors did not make extensive comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was addressed in the sensitivity analysis in which cost and clinical estimates were varied. The study referred to patients with MESCC and this was reflected in the authors’ conclusions. Some results were presented selectively, for example the total costs were not reported.

**Implications of the study**

The study results suggest that S+RT could represent good value for money for the treatment of MESCC. However, the authors pointed out that the value that society places on ambulatory function represents a key issue in the economic evaluation of treatments for MESCC.
Source of funding
None stated.

Bibliographic details

Other publications of related interest
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