Cost-utility analysis of a malignant glioma protocol
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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
A dose-escalating protocol of hyperfractionated twice-daily radiation therapy (RT) combined with carmustine in the treatment of malignant glioma. The doses considered were 64.8 Gy, 72.0 Gy, 76.8 Gy, and 81.6 Gy (at 1.2 Gy twice daily (b.i.d.)) and two accelerated doses of 48.0 and 54.4 Gy (at 1.6 Gy b.i.d.).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Patients with grade III or IV astrocytomas.

Setting
Hospital. The study was carried out in Toledo, USA.

Dates to which data relate
The effectiveness data were collected between 1983 and 1989. The unit costs were derived from a publication from 1994, whereas the date of the price data was not clearly stated.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was retrospectively undertaken using a model of charges and was not based on actual cost data.

Study sample
Power calculations were not used to determine the sample size. Although a total of 786 patients (randomized to treatment groups) were included in the study, only 747 were ‘evaluable’, with 78 patients randomised to the 64.8 Gy group, 158 to the 72.0 Gy group, 86 to the 76.8 Gy group, 120 to the 81.6 Gy group, 168 to the 48.0 Gy group, and 137 to the 54.4 Gy group. The exclusion rate was 5%.

Study design
Randomized controlled trial. It was not reported whether the study was conducted in a single or in multiple centres. The
duration of follow-up was not explicitly reported.

**Analysis of effectiveness**

It was not explicitly reported whether the analysis was based on intention to treat or on treatment completers only. The primary health outcome of the study was the quality adjusted survival (QAS) calculated using the data collected on 15 neurologic signs and symptoms including the treatment morbidity. The groups were shown to be comparable in terms of pretreatment characteristics. The Kaplan-Meier method was used to estimate QAS.

**Effectiveness results**

The average QAS (months) were:

- 64.8 Gy, 15.6;
- 72.0 Gy, 20.8;
- 76.8 Gy, 10;
- 81.6Gy 13.7.

The 48 and 54.4 Gy groups had an average QAS of 13.1 and 13.4 months, respectively. Statistical analysis revealed that the 72 Gy group had a significantly better average relative to other groups (P<0.017) except for the 64.8 Gy group (P= 0.183).

**Clinical conclusions**

The authors concluded that "An advantage of the intermediate dose level of 72.0 Gy was identified for all patients. This improvement was, however, greatest in patients less than the age of 50 years and those with a performance status of >80. Little benefit is seen to escalating the total dose used for patients who present with a KPS of < 80".

**Modelling**

The costs were calculated using a model of charges. The model included Medicare reimbursement data in order to account for the technical and professional components of treatments. The model also assumed a complex level of service for the treatment planning, simulation, treatment devices, and treatment.

**Measure of benefits used in the economic analysis**

Quality adjusted life years (QALYs) were used as the measure of benefit by converting the QAS results from months to years.

**Direct costs**

No discount rate was reported. Quantities were not reported separately. The costs measured were those associated with operating costs and were derived from Medicare Charge data using Relative Value Units from the Medicare region IV (Toledo, Ohio) for 1994. A model of charges was used to derive total costs. The cost analysis was performed from the point of view of a payer (Medicare). The costs associated with chemotherapy and pretreatment workup were omitted from the analysis since they were thought to be common to all strategies. The price year was not clearly reported.

**Indirect Costs**

Not calculated.
Currency
No specific currency was mentioned since relative value units (RVU) were used as the base in cost calculations.

Sensitivity analysis
A scenario analysis was performed by assuming only one treatment plan, simulation, and set of blocks.

Estimated benefits used in the economic analysis
The QALYs for patients aged under 50 years were:
- 64.8 Gy, 2.41;
- 72.0 Gy, 3.0;
- 76.8 Gy, 1.48;
- 81.6 Gy, 1.83.

The 48 and 54.4 Gy groups for patients <50 years of age had QALYs of 1.4 and 1.81, respectively.

The QALYs for the patients aged over 50 years were:
- 64.8 Gy, 0.592;
- 72.0 Gy, 0.666;
- 76.8 Gy, 0.408;
- 81.6 Gy, 0.583.

The 48 and 54.4 Gy groups for patients aged over 50 years had QALYs of 0.84, and 0.658 respectively.

Cost results
The total RVUs for the groups were:
- 64.8 Gy, 252.53;
- 72 Gy, 272.19;
- 76.8 Gy, 287.11;
- 81.6 Gy, 302.63;
- 48 Gy, 166.65;
- 54.4 Gy, 182.17.

Synthesis of costs and benefits
The average cost (RVUs) per QALY was reported for each strategy and differentiated by age group (threshold 50 years). The RVU per QALY for the groups aged under and over 50 years was:
- 64.8 Gy, 119.03 (<50 years), 198.39 (>50 years);
- 72 Gy, 100.65 (<50 years), 276.85 (>50 years);
76.8Gy, 104.78 (<50 years), 426.47 (>50 years);
81.6Gy, 90.73 (<50 years), 423.71 (>50 years);
48 Gy, 193.99 (<50 years), 703.7 (>50 years);
and 54.4 Gy, 165.37 (<50 years), 519.10 (>50 years).

Authors' conclusions
This preliminary study found the treatment arm possessing the longest survival also had the lowest cost-utility for patients <50 years of age. The 54.4 Gy arm had the lowest cost-utility when sensitivity analysis was performed closely approximating the 72.0 Gy arm for patients aged less than 50 years. The lowest cost-utility in the groups aged more than 50 years occurred in patients treated with accelerated fractionation to a total dose of 48 Gy.

CRD COMMENTARY - Selection of comparators
No comparator was introduced in the study.

Validity of estimate of measure of benefit
The estimate of the measure of benefit is likely to be internally valid.

Validity of estimate of costs
Since costing was not performed on the same patient sample and was, therefore not subject to randomisation, there may be some doubts as to the internal validity of the estimates of costs. Adequate details of methods of cost calculations were not given.

Other issues
The issue of generalisability to other settings or countries was not addressed. The authors reported this study as unique in the sense that no prior similar study was known to be available for comparison.

Implications of the study
Further studies, with a prospective collection of economic and quality of life data over the clinical trial, are needed in order to validly state the most efficient treatment option for malignant glioma patients.

Source of funding
None stated.

Bibliographic details

PubMedID
9336135

Indexing Status
Subject indexing assigned by NLM

MeSH
Brain Neoplasms /economics /radiotherapy; Cost-Benefit Analysis /methods; Glioma /economics /radiotherapy; Health Care Costs; Health Services Research /methods; Humans; Middle Aged; Quality-Adjusted Life Years; Radiotherapy Dosage; United States

AccessionNumber
21997001376

Date bibliographic record published
31/01/1999

Date abstract record published
31/01/1999