Optimal management when unsuspected N2 nodal disease is identified during thoracotomy for lung cancer: cost-effectiveness analysis

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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
The use of two strategies for the treatment of patients in whom non-small-cell lung cancer (NSCLC) metastatic to N2 lymph nodes was identified intraoperatively, prior to formal lung resection. The strategies were initial resection versus neoadjuvant therapy followed by resection (no initial resection). Patients undergoing neoadjuvant therapy received 2 cycles of chemotherapy with two agents and 50-Gy radiation therapy.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients in whom NSCLC metastatic to N2 lymph nodes was identified intraoperatively.

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

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1990 and 2002. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies.

Modelling
A simple decision analysis model was developed to assess the cost-effectiveness of the two treatment strategies under evaluation. The structure of the tree was reported. The model was deterministic.

Outcomes assessed in the review
The outcomes assessed in the initial resection group were:

operative mortality;
the probability of postoperative radiation therapy (RT) and postoperative chemoradiotherapy (CRT);
survival after resection alone; and
survival after resection and adjuvant therapy.
The outcomes assessed in the no initial resection group were:
operative mortality for exploration and for subsequent resection;
the likelihood of subsequent resection;
survival after neoadjuvant therapy and resection; and
survival after neoadjuvant therapy alone.
Also assessed were quality of life during postoperative recovery, RT, neoadjuvant or adjuvant CRT, and quality of life after all therapy had been completed.

**Study designs and other criteria for inclusion in the review**
The design of the primary studies was not reported. Reports published in English from 1990 to 2002 were eligible for inclusion in the review. Articles were selected if they had at least 25 patients in each surgical candidate group and median survival and operative mortality were reported (or calculable) for N2 patients.

**Sources searched to identify primary studies**
MEDLINE was searched for relevant primary studies using the keywords ("lung resection" and "lung neoplasm") and ("stage III" or "stage IIIa" or "mediastinal adenopathy" or "N2").

**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**
Forty-five primary studies were included in the review.

**Methods of combining primary studies**
A meta-analysis of the primary estimates was conducted and the weighted mean survival was calculated.

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

**Results of the review**
In the initial resection group, the estimated values were 0.03 (range: 0.01 - 0.05) for operative mortality, 0.25 (range: 0.15 - 0.35) for the probability of postoperative RT, and 0.5 (range: 0.4 - 0.6) for the probability of postoperative CRT. Survival was 1.8 years (range: 1.2 - 2.4), both after resection alone and after resection and adjuvant therapy.
In the no initial resection group, the estimated values were 0.005 (range: 0.002 - 0.01) for operative mortality for exploration, 0.05 (range: 0.03 - 0.07) for operative mortality for subsequent resection, and 0.7 (range: 0.5 - 0.9) for the likelihood of subsequent resection. Survival was 2.6 years (range: 2 - 3.2) after neoadjuvant therapy and resection, and 1 year (range: 0.8 - 1.2) after neoadjuvant therapy alone.

The values of quality of life were 0.75 (range: 0.6 - 0.9) for postoperative recovery, 0.7 (range: 0.5 - 0.9) for RT, 0.65 (range: 0.5 - 0.8) for neoadjuvant or adjuvant CRT, and 0.85 (range: 0.75 - 0.95) after all therapy had been completed.

Methods used to derive estimates of effectiveness
Some assumptions were made for periods of decreased quality of life.

Estimates of effectiveness and key assumptions
Periods of decreased quality of life were assumed to be 0.1 years for postoperative patients who were to receive neoadjuvant or adjuvant therapy, 0.2 years for postoperative patients who did not receive neoadjuvant or adjuvant therapy, and 0.2 years for the administration of neoadjuvant or adjuvant therapy. No adjustment was made for quality of life at the end of life.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were derived from the decision model. No discounting was applied. The utility values were derived from published studies.

Direct costs
Discounting was not relevant due to the short life expectancy of the patients considered in the study. The unit costs and the quantities of resources used were not reported separately. The health services included in the economic evaluation were RT, CRT, resection, surgical exploration and operative mortality. The cost/resource boundary of the medical centre was used. The resource use data were based on probability values estimated from the review of the literature, which was conducted to derive the effectiveness values. The surgical costs were derived using actual data from a sample of 100 patients who underwent lung resection at the authors’ centre from 1998 to 2000. The other costs were estimated from published studies. All the costs were converted into 2002 values using the Consumer Price Index.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

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

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were conducted to investigate the robustness of the estimated cost-effectiveness ratios. One-way sensitivity analyses were performed on all model inputs, while two-way sensitivity analyses were conducted only on selected variables. The ranges used were derived from the literature.

Estimated benefits used in the economic analysis
The initial resection strategy led to 1.34 QALYs, while the no initial resection strategy resulted in 1.80 QALYs.
Therefore, the difference in QALYs gained was 0.45, favouring the no initial resection option.

Cost results
The estimated costs were $19,000 with initial resection and $27,000 with no initial resection. The difference of $8,000 favoured initial resection.

Synthesis of costs and benefits
Average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the two strategies.

The average cost per QALY was $14,193 with initial resection and $14,933 with no initial resection.

The incremental cost effectiveness ratio (ICER) was $17,119 with no initial resection relative to initial resection.

The ICER was well below the widely accepted threshold for cost-effectiveness ($50,000/QALY).

The results of the one-way sensitivity analysis showed that the survival estimates had the greatest impact on the estimated ICER. Above a survival estimate of 2.28 QALYs after initial surgery followed by adjuvant therapy, the ICER of no initial resection was above $50,000. Below a survival estimate of 2.07 QALYs after no initial resection followed by neoadjuvant therapy and resection, the ICER of no initial resection was above $50,000.

The two-way sensitivity analysis suggested that no initial resection was predominantly associated with favourable ICERs.

Authors’ conclusions
Neoadjuvant therapy followed by resection in patients with N2 nodal disease at the time of exploratory thoracotomy was cost-effective in comparison with initial resection. This result was mainly due to the beneficial effects of neoadjuvant therapy and the exclusion of patients with more aggressive disease from the surgical candidate pool.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The two strategies under evaluation represented two treatment options widely used for the study population considered in the study. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The measures of effectiveness were derived from a systematic review of the literature. A meta-analytic approach was used to combine the primary estimates and ranges of values, which were then used in the sensitivity analyses. The authors described the search and selection of the relevant primary studies in detail. However, the designs of the primary studies included in the review were not reported. The use of extensive sensitivity analyses was useful.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate for assessing the impact of the interventions on the patients’ health, as the strategies under evaluation affected both the length and quality of life. The use of QALYs enables comparisons to be made with the benefits of other health care interventions.

Validity of estimate of costs
The authors stated explicitly which perspective was adopted in the study. Given that perspective, it appears that all the relevant categories of costs have been included in the economic evaluation. However, the costs were reported in macro-
categories and were not broken down into detailed items. The price year was provided, which makes reflation exercises in other settings feasible. The source of the cost data was provided for each category of cost. The costs were treated deterministically in the base-case but were then varied in the sensitivity analysis.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were carried out, which enhanced the external validity of the analysis. The authors noted that the model did not consider the option for postoperative adjuvant chemotherapy, which is often offered to patients who complete neoadjuvant therapy but have residual nodal disease at the time of resection. However, this and other minor changes in the decision model would not change the conclusions of the analysis, owing to the large gap between the estimated ICER of no initial resection and the threshold of $50,000 per QALY.

Implications of the study
The authors suggested that their findings could enhance the relevance of preoperative staging before proceeding with lung resection.

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None stated.

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Other publications of related interest


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