Combined bronchoscopy, mediastinoscopy, and thoracotomy for lung cancer: who benefits

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 combined use of surgical staging (bronchoscopy and mediastinoscopy) and resection (thoracotomy) of lung cancer was examined. This combined strategy was compared with a strategy in which surgical staging was separated from the resection, resulting in two separate operations (staged strategy).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patient who had undergone bronchoscopy, mediastinoscopy and thoracotomy for resection of lung cancer.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness study was carried out between January 1998 and July 2001. The price year was not reported.

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

Link between effectiveness and cost data
It would appear that the costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
The sample size does not seem to have been determined in the planning phase of the study. In addition, power calculations do not appear to have been performed retrospectively. The patients were identified from the Thoracic Surgery Registry. During the study period, a total of 343 patients underwent bronchoscopy. Ninety-eight patients underwent the staged strategy, of which 41 received induction chemoradiotherapy. Three hundred and nineteen patients were to have all procedures under the same anaesthetic (combined). Of these, 297 received all procedures as planned, 286 as sole therapy and 11 after induction chemoradiotherapy. As a disproportionate number of patients received induction chemoradiotherapy in the staged group, which could bias comparisons, the analyses concentrated on the 57
staged and 286 combined patients in whom resection was the sole therapy. The authors did not report the age or gender mix of the two groups of patients.

**Study design**
The study appears to have been based on a prospective cohort study that was carried out in a single centre. The duration of follow-up was not explicitly reported, but it would appear to have been until the patient was discharged from hospital. The authors reported no loss to follow-up.

**Analysis of effectiveness**
All the patients included in the study were accounted for in the analysis. The primary health outcomes used were mortality and morbidity. Operative mortality was defined as death in-hospital or within 30 days of operation. Complications were classified as:

- pulmonary, which included reintubation, pneumothorax, adult respiratory distress syndrome, atelectasis requiring bronchoscopy, pneumonia, bronchopleural fistula, pulmonary embolism, and pleural effusion;
- cardiac, which included arrhythmia and myocardial infarction; or
- other, which included stroke, vocal cord paralysis, sepsis and bleeding.

The duration of the operation and total hospital stay were also recorded. The duration of the operation was calculated from anaesthesia induction until anaesthesia ended. For the staged strategy, the operative time was the sum of both procedures. Selection bias was addressed by constructing propensity scores. The probability of undergoing the combined versus staged strategy (propensity score) was estimated by a logistic regression incorporating 17 variables such as age, gender, prior cardiac surgery, clinical tumour and weight loss. Sporadic missing values were imputed by taking the most frequent response category, or by averaging non-missing values. For each of the 57 staged patients, a well-matched combined patient was sought by propensity score matching, which yielded 54 well-matched pairs. The surgeon was also added to the 17-variable propensity model to yield a second propensity score. Using this score, 44-well matched pairs were identified. A multivariate logistic regression analysis, to identify risk factors for morbidity and mortality in all 343 patients, was then performed. The variables considered were the 18 used to develop a propensity score, plus treatment strategy, type of operation and tumour histology, amongst others.

**Effectiveness results**
Operative mortality and morbidity were similar for the staged and combined strategies. When the groups were not matched, the operative mortality was 1.8% (n=1) in the staged group and 2.1% (n=6) in the combined group, (p=0.9). Morbidity was 28% (n=16) in the staged group and 30% (n=85) in the combined group, (p=0.8).

When the groups were matched without surgeon, the operative mortality was 0 in the staged group and 3 (5.6%) in the combined group, (p=0.08). Morbidity was 26% (n=14) in the staged group and 33% (n=18) in the combined group.

When the groups were matched with surgeon, there was no operative mortality in either of the two groups. Morbidity was 20% (n=9) in the staged group and 34% (n=15) in the combined group.

Several factors were associated with increased mortality and morbidity. These were male gender (odds ratio, OR=2.00, p=0.006), worsening Eastern Cooperative Oncology Group performance status (OR=1.52, p=1.52) and increasing pathological N classification (OR=1.73, p=0.003).

The median operative time was less for the combined strategy than the staged strategy, irrespective of whether the groups were propensity matched, but the median hospital stay was similar, (p>=0.1).

**Clinical conclusions**
The study demonstrated comparable operative mortality and morbidity with either a staged or combined strategy.
Measure of benefits used in the economic analysis
No summary measure of benefit was derived. In effect, the study was a cost-minimisation analysis.

Direct costs
The direct costs of the hospital were included in the analysis. These were for anaesthesia, surgery, pathology, nursing, pharmacy, radiology, and other miscellaneous costs. The nursing costs covered the operating room, intensive care unit, hospital and rehabilitation. The costs were obtained from the hospital's cost accounting system. The resource quantities and the costs were not reported separately. Discounting was unnecessary since all the costs were incurred during a short time, and was not performed. The cost of the staged strategy was expressed as a percentage of the costs of the combined strategy. For propensity-matched pairs, the relative cost was the ratio of each matched pair. For overall data, all combinations of patient pairs (n=16,302) were used and the resulting ratios were summarised. The authors also calculated the net revenue. This was the payment expected, calculated as charges less contractual insurance adjustments plus patient co-pay. The revenue of the staged strategy was expressed as a percentage of the combined strategy.

Statistical analysis of costs
Continuous variables, such as costs, were compared using appropriate t-tests, the Wilcoxon rank-sum test, or the Cox proportional hazards test. All statistical tests were two-sided.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
As the costs and revenue of the staged strategy were expressed as a percentage of those of the combined strategy, the costs were not expressed in monetary terms.

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The median relative direct costs were greater for the staged strategy in the unadjusted and propensity-based comparison without surgeon, (p<0.001). However, in the comparison with surgeon, the costs were similar because the combined cost was 15% higher than in the non-surgeon-matched group, and the staged cost was 6% lower. The median net revenue was higher for the staged strategy.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
The combined strategy provided efficient, safe health care for clinically operable lung cancer patients, but it might not be as financially rewarding for the hospital as a staged strategy.
CRD COMMENTARY - Selection of comparators

Although no explicit justification was given for the comparator used, it would appear to represent current practice in the authors’ setting. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness

It was unclear whether the study was based on a retrospective or prospective cohort study, as the authors only reported that the patients were identified from the Thoracic Surgery Registry. Ideally, the study would have been a prospective cohort study, which is less prone to selection bias. The authors failed to show whether the patient groups were comparable at analysis in terms of their age and gender. However, the authors matched groups according to a propensity score (which included up to 18 different variables), thus ensuring that similar patients were compared. This approach also ensured that selection bias was addressed. The study sample appears to have been representative of the study population. Appropriate statistical analyses were undertaken to test for any statistically significant differences between the two groups. In addition, regression analyses were undertaken to identify risk factors for morbidity and mortality in all 343 patients who had undergone bronchoscopy, mediastinoscopy and thoracotomy for resection of lung cancer. The authors made some attempts to enhance the internal validity of the study. However, given the study design, the overall internal validity is likely to be quite poor.

Validity of estimate of measure of benefit

The authors did not derive a summary measure of health benefit. The study was, in effect, a cost-minimisation study.

Validity of estimate of costs

All the categories of cost relevant to the perspective adopted were included in the analysis. However, some individual cost items were omitted from the analysis, for example, physician fees. As the median operative time was lower for the combined strategy group, it would appear that excluding these costs would act in favour of the staged strategy group, which had longer operative times and thus higher physician input. The costs and the quantities were not reported separately, which will limit the generalisability of the authors’ results. The authors also failed to report the total costs for each group, simply reporting the costs of the staged strategy as a percentage (ratio) of those of the combined strategy. Again, this will limit the generalisability of the results. The cost information was derived from the hospital’s accounting system. An appropriate statistical analysis of the costs was performed. Discounting was unnecessary since all the costs were incurred during one year. The authors also calculated the payment expected for the operation. The date to which the prices related was not reported.

Other issues

The authors did not make appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was not addressed, and the authors warned the reader that their study might not be generalisable since it was conducted in a single institution. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. A number of further limitations to the study were reported. For example, the study was limited by a lack of randomisation, which was possible despite the inability to blind the team to strategy. Further, contemporary methods for generating quasi-randomised comparison, such as those used in this study, were limited by an inability to account for unrecorded variables and to separate confounding between surgeon and strategy.

Implications of the study

The authors recommended that any patient who is medically operable and has clinical Stage I or II non-small-cell lung cancer should be offered a combined strategy. However, if mediastinoscopy reveals unanticipated mediastinal nodal metastases, this strategy should be abandoned.

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