What is the best management strategy for high grade dysplasia in Barrett's oesophagus: a cost effectiveness analysis

Shaheen N J, Inadomi J M, Overholt B F, Sharma P

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
Three strategies for treating patients with Barrett's oesophagus (BO) with high-grade dysplasia (HGD) were examined. The strategies were elective surgical oesophagectomy (ESO), endoscopic ablation (EA), and surveillance endoscopy (SE). SE was performed every 3 months as long as HGD was detected, and for at least one year. If no HGD was detected in subsequent surveillance, the intervals were lengthened to every 6 months for one year, then yearly thereafter. A finding of cancer led to oesophagectomy. The EA approach considered in the analysis was photodynamic therapy.

Type of intervention
Screening and treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 50-year-old Caucasian male patients with symptoms of reflux prompting endoscopy, whose results demonstrated BO with HGD. Patients with co-morbid conditions precluding oesophagectomy were excluded.

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

Dates to which data relate
The effectiveness data were derived from studies published between 1983 and 2003. No dates for the resource use data were reported. The price year appears to have been 2001.

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

Modelling
A hybrid model of a linear decision tree that terminated in a Markov model was constructed to determine the costs and benefits associated with the alternative strategies under examination. The patients were assigned to no preventive care or to one of the three treatment strategies. In the ESO branch, patients underwent the procedure with the associated morbidity and mortality, while those successfully cured lived the remainder of their life with a diminished utility. In the EA arm, patients underwent up to three attempts and several possible outcomes, including the risk of diminished utility. In the EA arm, patients underwent up to three attempts and several possible outcomes, including the risk of diminished utility. In the EA arm, patients underwent up to three attempts and several possible outcomes, including the risk of diminished utility.
surveillance. Finally, patients in the SE branch entered directly in the Markov model, which had yearly cycles. The patients were followed until the age of 80 years or death.

**Outcomes assessed in the review**
The outcomes derived from the literature were:

- the annual rates of progression from no dysplasia to cancer, from low-grade dysplasia (LGD) to cancer, from HGD to cancer, from no dysplasia to HGD, from LGD to HGD, and from no dysplasia to LGD;
- the annual rates of regression from no dysplasia to no BO, from LGD to no dysplasia, from HGD to no dysplasia, and from HGD to LGD;
- the probability values of ablation-related stricture,
- ablation-related perforation,
- eradication of all HGD with ablation,
- eradication of BO with ablation,
- surgical resectability and mortality (cancer diagnosed by surveillance or asymptomatically),
- major surgical morbidity,
- cure rate (cancer diagnosed by surveillance or asymptomatically),
- death from endoscopy,
- endoscopy-related major complications,
- mortality from surgery to repair perforation, and
- major morbidity from surgery to repair perforation;
- the misdiagnosis rates of dysplastic states, such as cancer called HGD or LGD, HGD called cancer or LGD, and LGD called cancer or HGD; and
- the utility values associated with BO, oesophagectomy, and cancer.

**Study designs and other criteria for inclusion in the review**
It was not stated whether a systematic review of the literature was carried out to identify relevant sources of data. The design of the primary studies was not reported. Some of the utility weights were derived from a study that used a visual analogue scale.

**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**
Fifty-two studies provided the data used in the decision model.

**Methods of combining primary studies**
If the data were of similar quality, meta-analytic techniques were used to combine the primary estimates. However, if the homogeneity test was failed, the largest reported cohort with the longest follow-up was used as the main source of data.

**Investigation of differences between primary studies**
A homogeneity test was used to investigate differences among the primary studies.

**Results of the review**
The annual rate of progression was 0.005 from no dysplasia to cancer, 0.025 from LGD to cancer, 0.025 from HGD to cancer, 0.01 from no dysplasia to HGD, 0.05 from LGD to HGD, and 0.05 from no dysplasia to LGD.

The annual rate of regression was 0.0175 from no dysplasia to no BO, 0.63 from LGD to no dysplasia, 0.10 from HGD to no dysplasia, and 0.07 from HGD to LGD.

The probabilities were:

- 0.185 for ablation-related stricture,
- 0.003 for ablation-related perforation,
- 0.88 for eradication of all HGD with ablation,
- 0.40 for eradication of BO with ablation,
- 0.95 for surgical resectability with cancer diagnosed by surveillance and 0.50 for surgical resectability with cancer diagnosed asymptotically,
- 0.027 for mortality with cancer diagnosed by surveillance and 0.05 for mortality with cancer diagnosed asymptotically,
- 0.15 for major surgical morbidity,
- 0.80 for cure rate with cancer diagnosed by surveillance and 0.20 for cure rate with cancer diagnosed asymptotically,
- 0.000021 for death from endoscopy,
- 0.0013 for endoscopy-related major complications,
- 0.08 for mortality from surgery to repair perforation, and
- 0.20 for major morbidity from surgery to repair perforation.

The misdiagnosis rate of dysplastic states was 0.175 for cancer called HGD, 0.05 for cancer called LGD, 0.11 for HGD called cancer, 0.115 for HGD called LGD, 0.083 for LGD called cancer, and 0.05 for LGD called HGD.

The utility value associated with BO was 1, with oesophagectomy 0.97, and with cancer 0.50.
Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were calculated using the decision model and discounted at an annual rate of 3%. The number of cancers associated with each option was also reported.

Direct costs
Discounting was relevant due to the long timeframe of the analysis and an annual rate of 3% was applied. The unit costs were not presented separately from the quantities of resources used and some costs were reported as macro-categories. The health services included in the economic evaluation were ablation therapy, endoscopy with biopsy, repair of oesophageal perforation, endoscopic palliation of unresectable cancer, surgical oesophagectomy, care of incurable cancer, clinic visit, and care of ablation-related stricture. The cost/resource boundary of the third-party payer was adopted. The costs were estimated using data derived from the Centers for Medicare and Medicaid Services of the US government. The source of the resource use data was not reported. The price year was presumably 2001.

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 ($) and Euros (Euro).

Sensitivity analysis
One- and two-way sensitivity analyses were carried out to investigate uncertainty due to variability in the data. Monte Carlo simulations were also performed, running 1,000 simulations. Almost all of the model inputs were varied. The ranges of values used in the sensitivity analyses were derived from the literature and the other sources used in the base-case analysis.

Estimated benefits used in the economic analysis
The discounted QALYs were 13.90 with no preventive strategy, 14.89 with ESO, 14.96 with SE, and 15.51 with EA. The number of cancers was 185.4 with no preventive strategy, 2 with ESO, 65.2 with SE, and 31.6 with EA.

Cost results
The discounted costs were $748 (Euro 613) with no preventive strategy, $34,857 (Euro 28,583) with ESO, $34,724 (Euro 28,474) with SE, and $41,998 (Euro 34,438) with EA.

Synthesis of costs and benefits
Average and incremental cost-utility ratios were calculated to combine the costs and benefits of the treatment strategies under examination. The average cost per QALY was $54 (Euro 44) with no preventive strategy, $2,341 (Euro 1,920) with ESO, $2,322 (Euro 1,904) with SE, and $2,708 (Euro 2,220) with EA. The incremental analysis showed that ESO was dominated by SE, while EA dominated (extended dominance) SE. The incremental cost per additional QALY with SE relative to no preventive strategy was $32,053 (Euro 26,283). The incremental cost per additional QALY with EA relative to no preventative strategy was $25,621 (Euro 21,009).

The sensitivity analysis showed that the results of the base-case were generally robust to variations in the base-case assumptions. The model was sensitive to variations in the transition probability from HGD to cancer. When such a
probability value increased, no prevention became a much less effective strategy. Only when the yearly rate of cancer in
the setting of HGD exceeded 30% (an unrealistic level) was surgery more effective than EA. On the cost side, the total
costs of EA should be less than $15,000 (Euro 12,300) for EA to be the most cost-effective strategy. The results of the
Monte Carlo simulation revealed that the incremental cost-utility ratio of EA was less than $50,000 (Euro 41,000)
relative to no screening or SE in more than 95% of the simulations. A tornado diagram showed that the utility of living
in the post-oesophageal state was the variable with the greatest impact on the cost-utility ratios.

Authors’ conclusions
Endoscopic ablative therapy using photodynamic therapy was a cost-effective strategy for the treatment of Barrett’s
oesophagus (BO) with high-grade dysplasia (HGD). Endoscopic ablation (EA) dominated surgery and most payers
could find it more efficient to use EA rather than surveillance endoscopy (SE) because a condition of extended
dominance existed.

CRD COMMENTARY - Selection of comparators
The comparators were selected on the basis of treatment strategies currently used for BO with HGD in the USA. The
option of no intervention was also considered for comparative purposes. You should decide whether they are valid
comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from published data. It was not stated whether a systematic review of the literature
had been undertaken and no information on the design of the primary studies was provided. Therefore, it is not possible
to determine the validity of the sources used. The authors reported the criteria used to combine the primary estimates
and acknowledged that, in some cases, it was not possible to combine the estimates because of heterogeneity among the
studies. The uncertainty in the estimates used in the model was investigated in the sensitivity analysis.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate because it captured the impact of the interventions
on quality of life and survival. Discounting was applied, as recommended in US guidelines. The QALYs were obtained
using the decision model. QALYs are easily compared with the benefits of other health care interventions.

Validity of estimate of costs
The perspective adopted in the study was explicitly stated. As such, all relevant categories of costs were included in the
analysis. However, a detailed breakdown of the cost items was not provided, which limits the possibility of replicating
the results of the analysis. The source of the costs was provided, but no information on resource consumption was
reported. The costs were treated deterministically in the base-case, but some estimates were varied in the sensitivity
analysis. The price year was implicitly reported, which will facilitate reflation exercises in other settings.

Other issues
The authors compared their findings with the results of a published model that reported similar conclusions to those
observed in the current analysis. The issue of the generalisability of the study results to other settings was addressed
only with respect to the patient population, which referred to a typical Caucasian male patient. It was unclear whether
the study results could be transferred to other patient populations. Some sensitivity analyses were performed, which
enhanced the external validity of the analysis. The authors noted both some strengths and drawbacks of the analysis.
The main advantages were that the model considered histological misdiagnosis of specimens, utility estimates were
derived from a sample of patients rather than from a group of experts, and transitions among health states reflected the
natural history of disease. However, it was noted that some model inputs were based on relatively short-term data, and
there was some variability in the published estimates.
Implications of the study
The study results supported the use of EA for the treatment of BO with HGD. The presence of extended dominance of EA over SE has ethical implications, and the final decision of the most cost-effective option depended on society's willingness-to-pay for such treatments.

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