Expandable metal stents versus laser combined with radiotherapy for palliation of unresectable esophageal cancer: a prospective randomized trial


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
Combined laser-percutaneous radiotherapy was compared with self-expanding metal stent for the treatment of patients with unresectable oesophageal cancer. The laser therapy was carried out using a flexible endoscope (GIF-2T 10; Olympus) under mild sedation with midazolone (5 - 15 mg) administered intravenously. The laser was a Nd:YAG (SLT CL 100; Surgical Laser Technology). The metal stent was a Wall-Stent (Schneider AG) of internal diameter 16 mm and length 10 cm. During the study, the stent was altered to an 11-cm Wall-Stent (Telestep Device; Schneider AG) with a polyurethane coating and of internal diameter 20 mm.

Type of intervention
Palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with unresectable oesophageal cancer. No inclusion or exclusion criteria were reported.

Setting
It was not explicitly stated where the study was set, although it appears to have been set in secondary care.

Dates to which data relate
The effectiveness data were collected between 1 January 1992 and 31 December 1994. It was unclear as to what year the cost data referred to. Also, a price year was not given.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
It was unclear whether the costing was carried out prospectively or retrospectively. The costs were reported as the "overall costs (per patient)". However, it was not clear whether these costs related to the same patient sample as the effectiveness data.

Study sample
The authors did not report whether power calculations were undertaken to estimate the number of patients required in
each arm of the study. The study sample comprised 39 consecutive patients with unresectable oesophageal cancer, which was appropriate for the stated objective. No details were given as to how the sample was selected. However, given the nature of the illness and, therefore, the potentially small number of available patients, it may be that all patients in the setting were eligible to enter the study. Informed consent was obtained for all patients.

Of the 39 patients included, 21 received the combined laser and radiation therapy (group 1). The mean age of these patients was 66.0 years (range: 45 - 83) and 80.95% were men. The remaining 18 patients received stents. The stent group was further divided into those who underwent partial laser therapy to reopen the lumen (due to complete obstruction). Within the stent group, 8 patients received laser therapy in addition to the stent (group 2a) and 10 received the stent alone (group 2b). The patients in group 2a had a mean age of 64.3 years (range: 42 - 79) and 87.5% were men. The patients in group 2b had a mean age of 67.6 years (range: 39 - 82) and 80.0% were men.

Tests were carried out to assess whether differences between the groups were statistically significant. The authors reported that the patients in the two arms of the trial were "comparable" in terms of their age and gender distribution. The authors did not report whether any patients refused to participate. They also did not report any exclusion criteria or whether any patients were excluded. This may have been because all patients with unresectable oesophageal cancer were considered eligible for inclusion. This possibility is supported by the fact that 39 consecutive patients were enrolled.

Study design
The study was a randomised controlled trial, but the method of randomisation was not reported. It was unclear whether the study was carried out in a single centre or multiple centres. The length of follow-up was not explicitly stated. Survival data (reported in months) were given as part of the results, thus the reader may infer that the patients were followed until death. Survival was reported to be longest in group 1, where the average survival, and therefore length of follow-up, was 7.9 months. No loss to follow-up was reported.

The nature of the treatment meant that blinding to the patients and physicians was not possible. The authors did not suggest that those responsible for the data collection or analysis were blinded.

Analysis of effectiveness
The basis of the analysis was intention to treat. The primary health outcomes were the grade of dysphagia, rate of restenosis, number of complications, fistula formation, bleeding, treatment-related mortality, length of hospital stay and length of survival.

The comparability of the two treatment groups was assessed statistically. There were some differences between the patients in the two arms of the trial, particularly in terms of the location of the tumours (group 1 was reported to have more patients with tumours located in the lower-third of the oesophagus). Despite this, there was no discussion or analysis of confounding factors.

Effectiveness results
The results were given as the mean and standard deviation (SD) for each of the outcome measures. Differences between the outcomes for each group (and confidence intervals) were not explicitly reported although the authors did report p-values for the difference in outcomes between the groups.

- Group 1 patients had a mean hospital stay of 30.0 (SD=5.4) days and survival of 7.9 (SD=2.6) months. The average grade of dysphagia in this group was 0.48 (SD=0.12) and restenosis occurred in 9 patients (43%).

- Group 2a patients had a mean hospital stay of 18.9 (SD=4.2) days and survival of 7.1 (SD=3.1) months. The average grade of dysphagia in this group was 0.38 (SD=0.1) and restenosis occurred in 3 patients (16.6%).

- Group 2b patients had a mean hospital stay of 7.1 (SD=3.1) days and survival of 6.83 (SD=2.6) months. The average grade of dysphagia in this group was 0.4 (SD=0.13) and restenosis occurred in one patient (5.5%).
There was no significant difference between the grade of dysphagia or survival between group 1 and groups 2a and 2b.

There was a significant difference, (p=0.05), between groups 1 and 2a for rate of restenosis and hospital stay.

There was a significant difference, (p=0.001), between groups 1 and 2b for rate of restenosis and hospital stay.

Adverse events were well documented by the authors.

Following stent placement, patients with a tumour in the upper-third suffered from respiratory distress, but in no case required respirator treatment. All resolved spontaneously after a few days.

In group 1, two severe bleeding episodes occurred. One case was stopped using laser coagulation, but the other patient died due to uncontrollable haemorrhage.

In group 1, oesophago-respiratory tract fistula was observed in two patients. This was treated with stent placement or insertion of a "fistula tubus" (balloon prosthesis). One of these patients died of recurrent aspiration.

Clinical conclusions
The authors focus on the equivalent length of survival in the two groups and the treatment complications (particularly those leading to death) observed in group 1. They conclude that "if 2 therapeutic modalities create the same survival rate, that treatment is to be applied which has less effect on life quality". Given the context of this comment, it is implicit that this statement gives a preference towards the treatment with the least detrimental effect on life quality, that is, treatment with stents.

Measure of benefits used in the economic analysis
No measure of benefit was used in the economic analysis. The authors did not report any attempt to compare a composite measure of the relative costs and benefits of the two treatments. As such, the economic analysis was based on a cost-consequences approach.

Direct costs
The cost per patient appears to have been estimated from the perspective of the hospital. The cost estimate was reported to include hospital day charges, and the costs for endoscopic treatment and radiotherapy. However, the cost per patient given in the analysis was not broken down to reflect these components. Discounting was not reported to have been undertaken. However, it may have been irrelevant since the length of follow-up appears to have been less than one year. The quantities and the costs were not reported separately.

It is unclear from the cost estimates whether they were derived using the actual costs and resources used by the patients, or whether they were based on published sources. The dates for which costs were estimated were not reported, and neither was the price year for the costs.

Statistical analysis of costs
No statistical analysis of the costs was reported.

Indirect Costs
The authors do not suggest that indirect costs were included. The treatments under consideration were relevant for palliative care. The patients were unlikely to have been sufficiently well to carry out economically productive work. Therefore, if the indirect costs were based on productivity, there would have been no indirect costs relevant to the treatment of these patients.

Currency
Austrian schillings (ATS).

**Sensitivity analysis**
No sensitivity analysis was reported.

**Estimated benefits used in the economic analysis**
Due to the cost-consequences approach adopted, see the 'Effectiveness Results' section.

**Cost results**
The overall cost per patient was ATS 257,349 (SD=6,325) in group 1, ATS 134,291 (SD=4,786) in group 2a, and ATS 55,780 (SD=6,827) in group 2b. It is not clear whether the costs of adverse effects were included within these cost estimates.

**Synthesis of costs and benefits**
The costs and benefits were not combined, which is consistent with the cost-consequences approach taken.

**Authors' conclusions**
The authors suggested that, since survival was "identical" in the two groups and group 1 had more treatment-related complications (including two deaths), stent treatment (with laser treatment where necessary) is the preferred treatment. The authors also drew the readers' attention to the "economic aspects" of treatment with self-expanding metal stents with or without prior laser treatment, referring to the cheaper costs associated with this treatment.

**CRD COMMENTARY - Selection of comparators**
The comparators were appropriate for the study. The authors fully justified their choice with reference to current practice and new treatments becoming available. Although not explicitly stated, current practice appeared to be laser-percutaneous radiotherapy. The expandable stents used in the analysis were reported to be a new class of stent and so represented a novel health technology.

**Validity of estimate of measure of effectiveness**
The analysis used randomised controlled trial. This was appropriate for the study question but some details, such as the method of randomisation and sample size determination, were not provided. The study sample appears to have been representative of the study population, as it comprised patients with unresectable oesophageal cancer. However, the patients were not shown to be comparable in terms of the location of their tumours. This may have biased the results, as tumour location may have been related to outcome. Eight patients in the laser plus stent group who had almost complete obstruction of the oesophageal lumen underwent partial laser therapy to reopen the lumen. The authors addressed this potentially confounding factor by forming two sub-groups (groups 2a and 2b), and helpfully provided results separately for the two groups. Several measures of benefit were considered. These included aspects relevant to the quality and quantity of life.

**Validity of estimate of measure of benefit**
No summary measure of benefit was estimated. The study was, therefore, categorised as a cost-consequences analysis. However, the authors implied that treatment with stents was a dominant treatment alternative since they reported that survival was equivalent, the complications were fewer, and the costs were lower.

**Validity of estimate of costs**
A perspective for the costs was not explicitly stated at the outset. However, it appears that the costs to the hospital were
the main focus. Three categories of cost were considered. These were hospital day charges, costs for endoscopic treatment and radiotherapy. These do not appear to cover the cost of any potential complications resulting from the treatment. The indirect costs were not included, but do not appear to have been relevant for the population considered. The cost differences between the treatment alternatives appear to be extensive. The costs to patients in group 1 were almost twice those for patients in group 2a, and nearly 5 times as great as those for patients in group 2b. The extent of the differences suggests that small adjustments made for the omitted costs may not alter the relative costliness of the three treatment possibilities.

Other issues
The sample size was very small (only 39 patients). In addition, no power calculation was undertaken to ensure sufficient patients in each arm of the trial, to rule out the influence of chance. Some of the outcome measures were found not to be statistically different between the groups of patients. However, this may have been related to the study having insufficient power to detect statistically significant differences. A larger study, or similar size study with a meta-analysis of the two sets of results, may help to reduce this element of uncertainty in future. The authors did not compare their results to prior studies of efficacy or cost. The issue of generalisability was not addressed. The authors did not appear to have reported the results selectively. The conclusions reflected the results of the analysis, and were possibly conservative since they did not refer to the difference in hospital stay, which was significantly less for treatment with stents. No limitations to the study were reported.

Implications of the study
The findings suggest that treatment of unresectable oesophageal cancer with self-expanding stents (either with or without prior laser treatment, is preferable to treatment with combined laser and radiotherapy treatment. However, the authors do not make any recommendations for policy or practice on the basis of the results of this study.

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None stated.

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Other publications of related interest


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