

Cost study of metal stent placement vs single-dose brachytherapy in the palliative treatment of oesophageal cancer

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Self-expanding metal stent placement and single-dose brachytherapy are commonly used for the palliation of oesophageal obstruction due to inoperable oesophagogastric cancer. We randomised 209 patients to the placement of an Ultraflex stent ($n = 108$) or single-dose brachytherapy (12 Gy, $n = 101$). Cost comparisons included comprehensive data of hospital costs, diagnostic interventions and extramural care. We acquired detailed information on health care consumption from a case record form and from monthly home visits by a specialised nurse. The initial costs of stent placement were higher than the costs of brachytherapy (€1500 vs €570; $P < 0.001$). Total medical costs were, however, similar (stent €11 195 vs brachytherapy €10 078, $P > 0.20$). Total hospital stay during follow-up was 11.5 days after stent placement vs 12.4 days after brachytherapy, which was responsible for the high intramural costs in both treatment groups (stent €6512 vs brachytherapy €7982, $P > 0.20$). Costs for medical procedures during follow-up were higher after stent placement (stent €249 vs brachytherapy €168, $P = 0.002$), while the costs of extramural care were similar (€1278 vs €1046, $P > 0.20$). In conclusion, there are only small differences between the total medical costs of both palliative treatment modalities, despite the fact that the initial costs of stent placement are much higher than those of brachytherapy. Therefore, cost considerations should not play an important role in decision making on the appropriate palliative treatment strategy for patients with malignant dysphagia.

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The incidence of oesophageal cancer has risen rapidly, due to a marked increase in the incidence of adenocarcinoma (Devesa *et al*, 1998; Botterweck *et al*, 2000). Oesophageal cancer is a disease with a high mortality, as reflected by a 5-year survival of 10–15% (Pisani *et al*, 1999). Moreover, more than 50% of patients with oesophageal cancer have already inoperable disease at presentation. Most of these patients require palliative treatment to relieve progressive dysphagia (Sagar *et al*, 1994). Treatment options presently available for palliation of dysphagia include self-expanding metal stent placement (Kozarek *et al*, 1996; Bartelsman *et al*, 2000; Siersema *et al*, 2001), laser therapy (Dallal *et al*, 2001), photodynamic therapy (PDT) (Luketich *et al*, 2000; Moghissi *et al*, 2000), external beam radiation in combination with brachytherapy (Taal *et al*, 1996; Schraube *et al*, 1997), brachytherapy as a sole treatment (Jager *et al*, 1995; Sur *et al*, 2002; Homs *et al*, 2003a) and dilatation (Lundell *et al*, 1989). A disadvantage of laser therapy is that repeated treatment sessions are required to achieve and maintain adequate palliation (Dallal *et al*, 2001; Spencer *et al*, 2002). A combined treatment of external beam radiation with brachytherapy is often too intensive for patients with inoperable disease due to metastases or a poor medical condition. Photodynamic therapy involves the local destruction of tumour tissue by light of a specific wavelength activating a previously administered

photosensitiser, which is retained in malignant tissue. Due to the high costs of the treatment, the side effects and the necessity of repeated treatments every 6–8 weeks, PDT is not considered to be the most optimal treatment for palliation of malignant dysphagia (Lightdale *et al*, 1995). Dilatation can relieve dysphagia temporarily, but it often provides relief palliation for a short period. In many patients with inoperable disease, a stent is placed for the palliation of dysphagia. In addition, brachytherapy as a sole treatment is frequently used in Western Europe, South Africa, Japan and to a lesser extent in the USA. Both stent placement and brachytherapy have been proven to be effective in relieving dysphagia with a low complication rate, but recurrent dysphagia due to various causes is seen in 30–40% of patients (Brewster *et al*, 1995; Kozarek *et al*, 1996; Bartelsman *et al*, 2000; Siersema *et al*, 2001; Sur *et al*, 2002; Homs *et al*, 2003a).

In order to comprehensively assess the relative merits of the different palliative treatments of malignant dysphagia, health economic aspects should be incorporated. Remarkably, the economic implications of both stent placement and brachytherapy have been evaluated only in a few studies (Adam *et al*, 1997; Farndon *et al*, 1998; Nicholson *et al*, 1999; Dallal *et al*, 2001; O'Donnell *et al*, 2002). If costs were considered, these were only 'roughly' calculated (Dallal *et al*, 2001), using charges/fees and with little information about the differentiation of the costs. In addition, the number of patients incorporated in the studies was low (Farndon *et al*, 1998; Dallal *et al*, 2001; O'Donnell *et al*, 2002). In studies on costs, this may result in a high degree of distortion,

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because peaks in volumes of some expensive cost items can highly influence the average outcomes.

We aimed to study the total direct and indirect costs of brachytherapy and stent placement in the palliation of malignant dysphagia within the framework of a randomised trial. We present estimates of the full cost price, based on real resource use, in substantial patient groups.

MATERIALS AND METHODS

Study population

We performed a prospective study in three university hospitals and six general hospitals in the Netherlands. Between December 1999 and July 2002, 209 consecutive patients with dysphagia from inoperable carcinoma of the oesophagus or gastric cardia due to metastases and/or a poor medical condition were randomised to placement of a covered Ultraflex stent ($n=108$) or single-dose (12 Gy) brachytherapy ($n=101$). For brachytherapy, a flexible applicator (Bonvoisin-Gérard Esophageal Applicator, Nucletron, Veenendaal, The Netherlands) with a diameter of 10 mm was passed down the oesophagus. A single dose of 12 Gy was administered with the radioactive source $^{192}\text{Iridium}$ at 1 cm from the source axis of the applicator. The study was approved by the Central Committee on Research Involving Human Subjects in the Netherlands.

Study end points

The clinical outcomes were functional outcome, complications, persisting or recurrent dysphagia needing re-intervention, survival and quality of life, as measured by standardised questionnaires. The clinical outcomes have been presented in detail elsewhere (Homs *et al*, 2003b, c). Here, we will focus on the real medical costs of the two treatment strategies. Costs were studied from a societal perspective and were estimated for the period after randomisation until death for 95% of the patients, or a follow-up of at least 9 months for the remaining 5% of patients.

Follow-up

Patients were prospectively followed by home visits of specially trained research nurses at 14 days, 1 month and then monthly until 1 year after treatment. After 1 year, patients were visited every 3 months, and/or telephone calls to the patient and/or the patients' general practitioner were made. For each patient, we registered the number of inpatient days, the time needed for nursing care and therapy as well as the visits to physicians and other health practitioners by a checklist filled in by the research nurse. The response was more than 90% during the entire follow-up period.

The participating clinicians filled out standardised case record forms (CRFs) during control visits, re-treatments and admissions.

Cost calculations

Real medical costs were calculated by multiplying the volumes of health care use with the corresponding unit prices. We made a distinction between the full cost price of the interventions of brachytherapy and stent placement by itself and the total medical costs per patient during follow-up.

The calculation of the full cost price of brachytherapy and stent placement consisted of detailed measurement of investments in manpower, equipment, materials, housing and overhead. The salary schemes of hospitals and other health care suppliers were used to estimate costs per hour for each caregiver. Taxes, social securities and vacations were included, as well as the costs of the time that could not be assigned to other patients. The costs of

equipment included those of depreciation, interest and maintenance.

For the calculation of the total medical costs per patient, we distinguished intramural medical costs (inpatient days, health practitioner activities, the full cost price of the medical treatment and other medical procedures) and extramural medical costs (home care, general practitioner). Costs caused by loss of production due to absence from work were not taken into account, because the majority of patients were retired from work.

For the most important cost items, unit prices were determined by following the micro-costing method (Gold *et al*, 1996), which is based on a detailed inventory and measurement of all resources used. For instance, we registered the time investments of health practitioners per patient (during the intervention). Costs for inpatient days in hospital were estimated as real, basic costs per day using detailed information from the financial department of the hospital. We made a distinction between the costs of general and university hospitals. These estimates included overhead and indirect costs. From a differential point of view, that is, comparison of the two treatment strategies, some diagnostic interventions were decided to be less relevant. We chose not to invest much time and effort in exploring costs that were unlikely to make any difference to the study result (Drummond *et al*, 1997), for example, because they were low in price or volume. For these items, we used charges as a proxy of real costs. In the Netherlands, a detailed 'fee for service' system is used for the remuneration of medical interventions and diagnostic procedures. In order to calculate the costs for medication, we used average charges for analgesics, antibiotics and additional medications.

Table A1 (Appendix A) gives an overview of the cost categories and data used in the cost calculations. We reported the costs in Euro for the year 2002, when 1 Euro equalised approximately 1 US dollar. Discounting was not relevant because of the limited time horizon (median survival 4–5 months).

Statistical analysis

All analyses were performed on an intention-to-treat basis. The cost differences between brachytherapy and stent placement were analysed using the Mann-Whitney U test. Since cost data per patient (but not per day care) are typically highly skewed, we used nonparametric bootstrap techniques to derive a 95% confidence interval for the differences in distributions of the direct medical costs.

In a sensitivity analysis, the effect of excluding 'palliation-related costs' was assessed by leaving these costs out of consideration. We performed calculations assuming that nursing home admissions and nursing care at home were not directly related to both treatments, but could be attributed to the advanced stage of the disease.

RESULTS

Patient characteristics and clinical outcomes

The two patient groups were comparable with respect to patient and tumour characteristics. Both treatment groups consisted predominantly of males, with a mean age of 69 years (Table 1).

Dysphagia improved more rapidly after stent placement than after brachytherapy. However, the overall improvement of dysphagia was better after brachytherapy. More complications occurred after stent placement (33% total complications *vs* 21% after brachytherapy; $P=0.02$). Major complications within 7 days after treatment included perforation ($n=3$), fever ($n=2$), severe pain ($n=2$) and aspiration pneumonia ($n=2$). Late major complications consisted predominantly of haemorrhage ($n=19$) occurring more frequently after stent placement (14 *vs* 5 after

Table 1 Characteristics of 209 patients randomised to brachytherapy or stent placement for palliation of malignant dysphagia

	Brachytherapy	Stent placement
Randomised	101	108
Age	69 ± 13	69 ± 11
Gender (male/female)	76/25	86/22
WHO performance score before treatment (mean ± s.d.)	1.0 ± 0.4	0.9 ± 0.5
<i>Indications for treatment</i>		
Metastases	66 (65%)	68 (63%)
Poor medical condition	23 (23%)	28 (26%)
Both	12 (12%)	12 (11%)
Tumour length (cm) (mean ± s.d.)	7.5 ± 2.6	7.5 ± 2.8
Received assigned intervention	96 (brachytherapy)	105 (stent)
Re-intervention	45 (stent) 3 (second brachytherapy)	2 (brachytherapy) 24 (second stent)
Median survival (days)	155 (95% CI: 128–182)	145 (95% CI: 104–186)
Total complications	23 in 21 patients (21%)	45 in 36 patients (33%)
Major complications	14 in 13 patients (13%)	28 in 27 patients (25%)
Minor complications	8 in 8 patients (8%)	16 in 16 patients (15%)
Persistent/recurrent dysphagia	53 in 43 patients (43%)	52 in 43 patients (40%)

brachytherapy). The need for re-intervention for persistent or recurrent dysphagia was not significantly different for both groups (40 vs 43%, respectively). Recurrent dysphagia after stent placement was predominantly caused by tumour overgrowth ($n=16$), stent migration ($n=18$) or food bolus obstruction ($n=16$), and was treated by placement of a second stent, endoscopic stent clearance or a variety of other treatments. The majority of re-interventions after brachytherapy were caused by tumour persistence ($n=18$) or tumour recurrence ($n=26$), both most frequently treated with placement of a stent.

The median survival was similar for both treatment groups (stent 145 vs brachytherapy 155 days). There was an overall long-term benefit in general (EORTC QLQ C-30 and EuroQol-5D) and disease-specific quality of life scores (EORTC OES-23) in the brachytherapy group during follow-up.

Costs

The initial cost price of treatment, based on real resource use, was much higher for stent placement (€1500) than for brachytherapy (€570). The main cause for this difference was the high purchase costs of the Ultraflex stent (€1100) (Table 2).

Table 3 gives an overview of the average health care use and costs per patient for stent placement and brachytherapy. Patients randomised to brachytherapy were admitted on average 7.1 days longer in a health care institution than patients randomised to stent placement (23.4 vs 16.3 days). The main reason for this was the longer period patients randomised to brachytherapy were admitted to nursing homes (11.0 vs 4.6 days). The average time spent in hospital was similar for both treatments (12.4 for brachytherapy and 11.5 for stent placement). The costs for intramural care were by far the highest cost category for both treatments, but differences were not statistically significant (stent placement €6512 vs brachytherapy €7982, $P>0.20$). Costs of medical procedures during follow-up were significantly higher for stent placement (€249) than for brachytherapy (€168) ($P=0.002$), since major complications and re-interventions occurred more often after stent placement than brachytherapy. The average costs for extramural care were €1278 for brachytherapy and €1046 for stent placement. For both treatments, this could largely be attributed to home visits by the general practitioner and specialised nursing care at home. The costs for medications were similar for brachytherapy and stent placement (€350 and €325).

Table 2 Full cost price (€, 2002) of brachytherapy and stent placement

Cost category	Brachytherapy	Stent placement
Personnel	152	74
Equipment	75	40
Materials	14	1307
Housing/overhead	70	40
Diagnostics	259	37
Total costs	570	1500

The total average costs per patient for both treatments were similar at €11195 for brachytherapy and €10078 for stent placement ($P>0.20$). If the 'palliation-related' health care was not taken into consideration, then the costs of intramural and extramural care for brachytherapy and stent placement decreased. This resulted in total medical costs for brachytherapy of €8490 and for stent placement of €8538 ($P>0.20$).

DISCUSSION

We found only small differences between the total medical costs of single-dose brachytherapy as compared to metal stent placement for the palliation of dysphagia from inoperable oesophageal carcinoma. Stent placement was initially more expensive than brachytherapy, due to the high purchase costs of the stent, but at the long term costs were comparable.

Many patients in both treatment groups needed re-intervention for persistent or recurrent dysphagia. Of the patients randomised to brachytherapy, 45 out of 101 (45%) subsequently received a stent, while 24 out of 108 (22%) of the patients randomised to stent placement received a second stent during follow-up. Since our analysis was based on the intention-to-treat principle, costs of non-assigned treatment were accounted to the randomised treatment group. Total treatment costs, which included the average costs of additional treatment plus re-intervention, were higher for stent placement. However, if the intramural and extramural health care costs were also taken into account, then these high initial costs were only a small part of the total medical costs, which resulted in similar total medical costs.

Table 3 Average health care use and costs (€, 2002) per patient for stent placement and brachytherapy

Cost category	Brachytherapy (n = 101)			Stent placement (n = 108)		95% CI ^a Mann-Whitney
	Cost price	Volume	Costs	Volume	Costs	
<i>Treatment</i>						
Brachytherapy	570	0.96	547	0,019	11	[253, 822] P < 0.001
Stent placement	1500	0.58	870	1,29	1935	
			1417		1946	
<i>Intramural care</i>						
Hospital (academic)	520	7.7	4006	6.9	3587	[-4341, 1104] P > 0.20
Hospital (general)	381	4.7	1788	4.6	1760	
ICU	1450	0.02	31	0.06	72	
Nursing home	173	11	1898	4.8	838	
Physician (academic)	135	1.41	190	1.30	176	
Physician (general)	98	0.70	69	0.82	79	
			7982		6512	
<i>Medical procedures</i>						
Endoscopy	125	0.74	93	1.17	146	[3, 137] P = 0.002
PEG	100	0.04	4	0.04	4	
X-ray thorax	37	0.78	29	1.41	52	
X-ray abdomen	37	0.07	3	0.21	5	
Ultra-sound abdomen	42	0.05	3	0.04	2	
X-ray oesophagus	37	0.13	5	0.19	7	
ERT	39	0.81	32	0.57	22	
Adjustment ERT	98	0.15	15	0.09	9	
			168		249	
<i>Extramural care</i>						
General practitioner (inpatient)	19	0,9	18	1,06	20	[-783, 227] P > 0.20
General practitioner (home visit)	37	9	333	8,1	298	
Nursing care at home (specialised)	55,6	13,4	750	11,4	638	
Nursing care at home	32,4	1,9	61	2	64	
Drip-feed	8,5	13,7	116	3,05	26	
			1278		1046	
<i>Medication</i>						
			350		325	
<i>Total costs per patient</i>			11 195		10 078	[-3790, 1806] P > 0.20

^aDerived from 2000 bootstrap samples drawn with replacement.

Cost comparisons between medical treatments are often based only on the initial costs. This would imply that stent placement, with the high purchase costs of the device, would be less attractive than brachytherapy. In this study, we clearly demonstrated that the total medical costs of stent placement and brachytherapy were similar when the full follow-up period was considered. This illustrates that cost comparisons between interventions may vary substantially, depending on which, and how many, components are included in a total cost equation (Sahai, 2000).

Few studies have been published on costs of brachytherapy or stent placement in the palliative treatment of oesophageal cancer. Three studies compared stent placement with plastic endoprostheses (O'Donnell *et al*, 2002), conventional therapy (Nicholson *et al*, 1999) or thermal ablative therapy (Dallal *et al*, 2001). These three studies reported corresponding initial costs for stent placement, but found lower total medical costs, compared to our study. Dallal *et al* (2001) included only the costs of the intervention and hospital stay in the total costs for stent placement (€4920), which can explain the difference in total costs compared to our study. They found a median hospital stay of 12 days after stent placement, similar to findings in our study (Table 3). Farndon *et al* (1998) compared the placement of a plastic endoprosthesis with single-dose brachytherapy and showed that the total costs of brachytherapy (€2603) were lower compared to stenting (€3564). Presently,

plastic endoprostheses are no longer considered adequate for palliation of malignant dysphagia due to a high procedure-related complication rate with plastic endoprostheses (Siersema *et al*, 1998). Since there is no detailed information available on the costs in the above-mentioned articles (Farndon *et al*, 1998; Nicholson *et al*, 1999; Dallal *et al*, 2001; O'Donnell *et al*, 2002), it is not possible to explain the differences in total costs between these studies and ours. It could well be that both intramural and extramural health care use was under-reported. Finally, the number of patients included and receiving stent placement or brachytherapy was relatively low ($n < 35$) in these studies (Farndon *et al*, 1998; Nicholson *et al*, 1999; Dallal *et al*, 2001; O'Donnell *et al*, 2002).

A common problem when using clinical trials for any kind of cost assessment arises from the fact that the clinical protocol mandates more visits, consultations and examinations than otherwise used in clinical practice (Myrvold *et al*, 2001). For a treatment in a research setting, there will be more costs, compared to daily practice. Therefore, we excluded protocol-driven medical care such as visits of the nurses from our cost calculation. The main goal of these visits was, apart from giving advice to patients, registration of health care consumption and outcomes, which is, of course, not common practice in normal daily care of patients.

Despite the high costs involved, detailed cost studies in the treatment of malignant disease and palliative therapy have received little attention. This may be due to the inherent difficulties in performing such studies. Follow-up of patients with malignant disease is sometimes difficult since the mortality rate is high, particularly among patients receiving palliative therapy (McQuay & Moore, 1994). In a palliative setting, it is sometimes difficult to differentiate between health care consumption, which can be attributed to the palliative stage of the disease or only to the treatment modality. If palliation-related costs were excluded, we found a decrease in the total costs of both treatments, but this did not affect the final conclusion that the total costs for brachytherapy and stent placement were similar.

This study focused on costs and not on efficiency. The primary aim of both treatments is to palliate symptoms rather than to improve the survival of oesophageal cancer. Both treatments resulted in an improvement of an important symptom of inoperable oesophageal cancer, that is, dysphagia. As survival of the two treatment groups was comparable, we did not perform a formal cost-effectiveness analysis. Despite a less rapid relief of

dysphagia and a higher initial failure rate, brachytherapy was found to be an attractive alternative to stent placement in the palliation of malignant dysphagia, as brachytherapy was safer with fewer procedures needed for recurrent dysphagia (Homs *et al*, 2003b).

In conclusion, our study provides detailed insight into the total medical costs of two frequently used palliative treatments of dysphagia due to oesophageal cancer, that is, stent placement and brachytherapy. In spite of the higher initial costs for stent placement than for brachytherapy, total medical costs were similar. Therefore, cost considerations should not play an important role in decision making on the appropriate treatment strategy.

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Appendix A

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Table A1 Cost categories and data used in cost calculations

Cost category	Parameter	Data collection health care use		Cost estimate (Unit price)
		CRF (physician)	Questionnaire (nurse)	
<i>Treatment</i>				
Brachytherapy	Number	*		Real costs
Stent placement	Number	*		Real costs
<i>Inpatient days</i>				
Hospital (academic)	Days	*	*	Real costs
Hospital (general)	Days	*	*	Real costs
ICU	Days	*	*	Real costs
Nursing home	Days		*	Charges
<i>Health practitioner (inpatient)</i>				
Physician (academic)	Visits	*	*	Real costs
Physician (general)	Visits	*	*	Real costs
<i>Medical procedures</i>				
Endoscopy	Number	*		Real costs
PEG	Number	*		Charges
X-ray thorax	Number	*		Charges
X-ray stomach	Number	*		Charges
Ultra-sound scan stomach	Number	*		Charges
X-ray oesophagus	Number	*		Charges
ERT	Number	*		Charges
Other therapy	Number	*		Charges
<i>Extramural care</i>				
General practitioner (inpatient)	Visits		*	Fees
General practitioner (home visit)	Visits		*	Fees
Nursing care at home	Number		*	Charges
Nursing care at home (specialised)	Number		*	Charges
Drip-feed	Days		*	Charges