Diseases of the Esophagus (2012) **25**, 410–415
DOI: 10.1111/j.1442-2050.2011.01248.x

DISEASES OF THE ESOPHAGUS

Original article

Combined stent insertion and single high-dose brachytherapy in patients with advanced esophageal cancer – results of a prospective safety study

H. Bergquist,[1] E. Johnsson,[2] J. Nyman,[3] H. Rylander,[3] E. Hammerlid,[1] S. Friesland,[4] H. Ejnell,[1] L. Lundell,[5] M. Ruth[1]

Departments of [1]ENT/H&N Surgery, [2]Surgery, and [3]Oncology, Sahlgrenska University Hospital, Gothenburg, and Departments of [4]Oncology and [5]Surgery, Karolinska University Hospital, Stockholm, Sweden

SUMMARY. **Previous randomized studies comparing the two commonly used palliative treatments for incurable esophageal cancer, i.e. stent insertion and intraluminal brachytherapy, have revealed the pros and cons of each therapy. While stent treatment offers a more prompt effect, brachytherapy results in more long-lasting relief of dysphagia and a better health-related quality of life (HRQL) in those living longer. This prospective pilot study aimed to explore the feasibility and safety of combining these two regimes and incorporating a single high dose of internal radiation. Patients with newly diagnosed, incurable cancer of the esophagus and dysphagia were eligible for inclusion, and stent insertion followed by a single dose (12 Gy) of brachytherapy was performed as a two-stage procedure. Clinical parameters including HRQL and adverse events were registered at inclusion, and 1, 2, 3, 6, and 12 months later. Twelve patients (nine males) with a median age of 73 years (range 54–85) were included. Stent insertion followed by a single dose of brachytherapy was successfully performed in all but one patient who was treated with stent only. Relief of dysphagia was achieved in the majority of cases (10/11, $P < 0.05$), but HRQL did not improve except for dysphagia-related items. Only minor adverse events, including chest pain, reflux, and restenosis, were reported. The median survival time after inclusion was 6.6 months. Our conclusion is that the combination of stent insertion and single high-dose brachytherapy seems to be a feasible and safe palliative regime in patients with advanced esophageal cancer. Randomized trials comparing the efficacy of this strategy to stent insertion or brachytherapy alone are warranted.**

KEY WORDS: **brachytherapy, dysphagia, esophageal neoplasm, palliative treatment, stent.**

INTRODUCTION

Esophageal cancer is usually diagnosed at a late stage. Regardless of whether the cancer is of squamous or columnar origin, the prognosis is dismal, with 5-year survival at around 10–15%.[1,2] The majority of patients are destined to receive palliation only, which is associated with a severely impaired health-related quality of life (HRQL).[3]

The main goal for such palliative treatment is to relieve dysphagia, and the two most commonly used strategies for improving swallowing are stent insertion or intraluminal brachytherapy. These two strategies were recently compared in Dutch and Swedish randomized studies.[3–5] While stent insertion had a prompt effect on dysphagia, treatment with brachytherapy results in a more durable effect on dysphagia and, in addition, a better HRQL. Both studies concluded that stent insertion should be offered to patients with a short life expectancy, while brachytherapy should be offered to those with a longer life expectancy. This view was also emphasized in a recent Cochrane review.[6]

Even though efforts have been made to find factors predictive of survival in this group of patients, the therapeutic choice for each individual patient remains a challenge.[7,8] Many unforeseen factors can arise, and a new strategy that exploits the advantages of both stent insertion and brachytherapy would therefore be appealing. The present pilot study aims to evaluate

Address correspondence to: Dr Henrik Bergquist, MD, PhD, Department of ENT/H&N Surgery, Sahlgrenska University Hospital, SE-41345 Gothenburg, Sweden. Email: henrik.bergquist@vgregion.se

the feasibility of combining these regimes in treating a single patient.

MATERIALS AND METHODS

Patients

To be eligible for inclusion in the study, patients were required to have biopsy-verified cancer of the esophagus or the gastroesophageal junction with an advanced tumor burden with known metastases (TxNxM1) or overgrowth on surrounding tissue (T4NxMx). Patients with TxNxMx could also be included if not eligible for curative treatment because of poor general condition (based on results from exercise ECG and spirometry in appropriate cases[9]) or patient noncompliance. The patients were also required to have dysphagia grade 2 or worse (according to Ogilvie *et al.*).[10] The exclusion criteria were an expected survival of less than 1 month, the presence of tracheoesophageal fistulae, tumor growth in the cervical part of the esophagus (making stent placement impossible), obstructing tumor with no ability to pass a probe, other concurrent significant malignancy and/or planned treatment with chemotherapy, or external radiotherapy due to esophageal malignancy.

Treatment

Stent insertion was performed using a self-expandable, covered Ultraflex® (Boston Scientific® Corp., Boston, MA, USA) metal stent with a length of 10–15 cm. All stents were inserted by use of standard techniques with or without predilation of the stricture.[11] As a second procedure, and with the intention to do this within 14 days, endoluminal brachytherapy was administered through the stent using a guidewire and a high-dose-rate Iridium[192] source with a 10-mm applicator (Nucletron Microselectron, Nucletron B.V., The Netherlands). The target was defined as the macroscopic tumor, to which was added a 1-cm therapeutic margin in both distal and proximal directions. Correct applicator placement was verified by X-ray examination. The dose was administered at a 10-mm depth from the surface of the applicator, and one fraction of 12 Gy was delivered. The stent insertion was performed under sedation, and the brachytherapy was performed under general anesthesia.

Clinical evaluation and follow up

At inclusion, and 1, 2, 3, 6, and 12 months later or until death, the Karnofsky's Index (0–100),[12] the dysphagia score according to Ogilvie *et al.*[10] (0 = no dysphagia; 1 = some dysphagia but no dietary limitations; 2 = can drink but only eat semisolid food; 3 = can only drink; and 4 = total dysphagia), weight, weight loss, and any adverse events were registered. The clinical follow up was completed as outpatient visits or through telephone conversations.

HRQL questionnaires

To measure HRQL, two established and standardized questionnaires were used.

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30, version 3.0), a cancer-specific questionnaire designed for self-administration, has been extensively used in different HRQL studies; its cross-cultural validity and psychometric properties are considered satisfactory.[13] The questionnaire comprises five functioning scales: physical, role, emotional, cognitive, and social functioning. There are three symptom scales (fatigue, nausea/vomiting, and pain) and six single items relating to dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties. The questionnaire also includes a global health status/quality of life (QL) scale (two questions). A 1-week time frame is employed. All scales and single-item scores are transformed to a score from 0 to 100. A high score for a functional scale and for the global health status/QL scale represents a high/healthy level of functioning/high QL, while a high score for a symptom scale or single item represents a high level of symptoms/problems. The QL scores are calculated according to the EORTC QLQ-C30 scoring manual.[14] A change of 10 or more in the mean score of a scale or item is considered clinically significant.[15,16]

The other questionnaire used was EORTC QLQ-Oesophageal Module 18 (OES18).[17] It consists of questions related to problems due to the esophageal cancer's location and treatment. The questionnaire comprises four scales: the dysphagia, eating, reflux, and local pain scales. There are six single items relating to problems with swallowing saliva, choking when swallowing, problems with dry mouth, problems with taste, problems with coughing, and problems with speech. Both the scales and single items are scored according to the same scoring system as is used for the EORTC QLQ-C30.[14]

The questionnaire was completed at inclusion and then mailed together with a preaddressed and stamped return envelope 1, 2, 3, 6, and 12 months later or until death.

Statistics and ethics

Frequencies and percentages were computed for categorical and dichotomous variables; means, standard deviation, median, and range were calculated for continuous variables. The Wilcoxon matched-pairs signed-rank test was used for tests between ordinal variables at inclusion and the various follow ups.[18] The

regional independent ethics committee approved the study protocol, and informed consent was obtained from the participants before inclusion in the study.

RESULTS

Twelve patients were recruited and included at the Sahlgrenska University Hospital (n = 8) and at the Karolinska University Hospital (n = 4). Nine patients were males; the median age was 73 years (range, 54–85). Demographics and tumor data are presented in Table 1. Two-thirds of the patients (8/12) were considered not to be eligible for curative treatment because of their poor general condition.[9] All patients suffered from dysphagia grade 2 or worse and reported an average weight loss of 10 kg compared with their habitual weight before the onset of the disease. Their median Karnofsky's Index was 80 (Table 2). The HRQL scores at inclusion were generally low and in conformity with the severity of the disease states (Fig. 1 and Table 3).

A self-expandable metal stent was inserted within a median of 6 days (range 1–14 days) after inclusion, followed by a single high-dose (12 Gy) of brachytherapy within a median of 9 days (range 1–11 days) after stent insertion. Brachytherapy was performed successfully in all but one case (patient no. 12), in whom technical difficulties prevented passage of the guidewire through the established stent to secure the position of the applicator. No other adverse event was reported for the initial combined stent and brachytherapy procedure.

At the 1-month follow-up visit, the majority of the patients (10/11) experienced relief of dysphagia compared with the pretreatment situation as measured by the Ogilvie dysphagia score ($P < 0.05$; Wilcoxon matched-pairs signed-rank test; Table 2). This improvement was generally maintained in patients still alive 1 and 2 months later. A corresponding clinically significant improvement was also found for the mean scores of the EORTC QLQ-OES18 dysphagia scale at the 1-, 2-, and 3-month follow-up visits. In addition, improvements were seen with respect to trouble swallowing saliva and problems with choking. Regardless of this, weight loss increased in most. The mean global quality of life (GQoL) score, as well as most of the other mean scores for the various scales and items of the EORTC QLQ-C30 and OES18 questionnaires, deteriorated over time. Because of the limited number of patients, only clinically significant changes in HRQL scores were evaluated.

No major adverse event occurred during the study period; however, minor complications included retrosternal pain that reverted spontaneously in five patients, transient vomiting in two patients, pneumonia that responded well to antibiotics in one patient, and restenosis that required an additional stent insertion 8 months after inclusion in one patient. None of the patients received additional chemo- or external radiotherapy. The median survival time after inclusion was 6 months and 18 days (Fig. 2 and Table 2).

DISCUSSION

The present study gives support to the feasibility and safety of combined stent insertion and single high-dose brachytherapy in patients with advanced and incurable esophageal cancer. The procedure was performed safely in the vast majority of patients, had a prompt effect on dysphagia, and was not burdened by any severe adverse events.

The potential advantage of combined stent and brachytherapy would be the potential synergy between the immediate relief of dysphagia and the longer term effects of endoluminal brachytherapy on HRQL. A finding that might be considered a bit unexpected, however, was that even though dysphagia improved in the majority of our patients, at least during the first months of follow up, weight loss

Table 1 Demographics and tumor data for the patients included

Pat no.	Age	Gender	Weight (kg)	Comorbidity	TNM	Histology	Location	Tumor length (cm)
1	54	F	62	–	T3N0M1	ac	Distal	11
2	57	M	46	alc	T4N1M0	scc	Mid	6
3	62	M	89	–	T3N1M1	ac	Distal	9
4	68	M	82	alc, liver failure, COPD	T4N1M0	scc	Prox	4
5	72	M	77	Crohn's disease	T3N1M0	scc	Mid	4
6	73	M	72	Diabetes, hypertension	T2N1M1	scc	Distal	6
7	74	M	61	–	T3N1M0	ac	Distal	7
8	82	F	45	Diabetes, hypertension	T3N1M0	ac	Distal	9
9	82	F	44	COPD	T3N0M0	scc	Mid	6
10	84	M	61	Atrial fibrillation	T3N1M0	scc	Distal	2
11	85	M	72	Angina pectoris	T2N1MX	scc	Distal	6
12	85	M	62	–	T3N1MX	scc	Mid	7

ac, adenocarcinoma; alc, alcoholism; COPD, chronic obstructive pulmonary disease; prox, proximal; scc, squamous cell carcinoma.

Table 2 Clinical data at inclusion and at the various follow ups and survival time after inclusion

Pat no	Parameter	Incl	1 mo	2 mo	3 mo	6 mo	12 mo	Survival time
1	Karnofsky	80	70	70	70	–	–	–
	Dysphagia	2	2	2	2	md	na	8 mo 5 d
	Weight loss	36	41	47	49	–	–	–
2	Karnofsky	80	80	80	80	60	–	–
	Dysphagia	3	1	1	1	1	na	8 mo 1 d
	Weight loss	15	11	10	11	16	–	–
3	Karnofsky	90	80	–	–	–	–	–
	Dysphagia	2	1	na	–	–	–	1 mo 17 d
	Weight loss	3	5	–	–	–	–	–
4	Karnofsky	80	80	–	–	–	–	–
	Dysphagia	3	2	md	md	na	–	5 mo 4 d
	Weight loss	5	5	–	–	–	–	–
5	Karnofsky	80	70	50	–	–	–	–
	Dysphagia	3	2	2	na	–	–	2 mo 28 d
	Weight loss	10	13	13	–	–	–	–
6	Karnofsky	100	80	–	–	–	–	–
	Dysphagia	2	1	na	–	–	–	1 mo 7 d
	Weight loss	10	10	–	–	–	–	–
7	Karnofsky	90	90	90	80	80	–	–
	Dysphagia	2	1	0	0	0	md	12 mo 5 d
	Weight loss	9	9	9	9	7	–	–
8	Karnofsky	70	70	50	–	–	–	–
	Dysphagia	3	2	3	na	–	–	3 mo
	Weight loss	9	10	12	–	–	–	–
9	Karnofsky	70	70	80	60	50	–	–
	Dysphagia	3	2	1	1	2	na	9 mo 27 d
	Weight loss	9	9	9	13	13	–	–
10	Karnofsky	60	70	60	–	–	–	–
	Dysphagia	3	1	1	na	–	–	2 mo 16 d
	Weight loss	5	9	11	–	–	–	–
11	Karnofsky	100	100	–	80	80	–	–
	Dysphagia	2	1	md	3	4	na	9 mo 20 d
	Weight loss	5	10	–	10	9	–	–
12	Karnofsky	80	80	–	–	–	–	–
	Dysphagia	3	2	md	md	md	na	11 mo 18 d
	Weight loss	20	21	–	–	–	–	–

Karnofsky's Index was scored according to established recommendations,[12] dysphagia grade was scored according to Ogilvie *et al.*,[10] and weight loss compared with habitual weight was recorded in kilograms. d, days; Incl, inclusion; md, missing data; mo, months; na, not applicable.

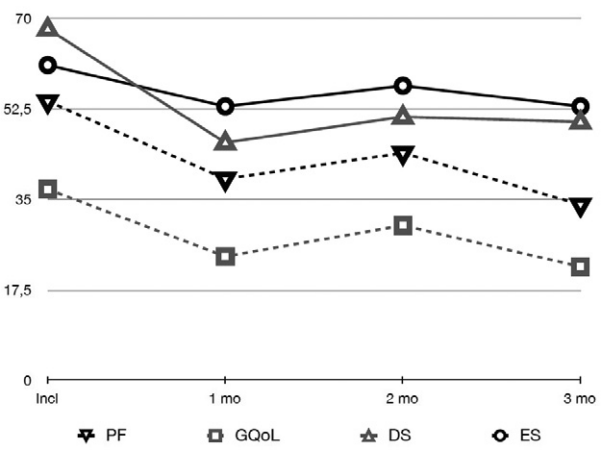

Fig. 1 Mean European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and EORTC QLQ-Oesophageal Module 18 (QLQ-OES18) scores at the inclusion (Incl) and at the 1, 2, and 3 months (mo) of follow ups. DS, dysphagia scale; ES, eating scale; GQoL, global quality of life; PF, physical functioning.

continued over time. In addition, the mean Karnofsky's Index, as well as most of the other mean scores for HRQL parameters, deteriorated throughout the study period. This, however, clearly reflects the advanced disease stage and rapid progress of malignant disease. Although swallowing-promoting measures may not result in weight gain, such interventions are of value for the general well-being of the patient.

Stent treatment has previously been combined with radiation, although mainly involving external radiotherapy and with somewhat discouraging results.[6] Only two small, earlier studies report the effects of the combination of stent insertion and internal radiation. Both were retrospective and reported diverging results.[19,20] In the study by Maier *et al.*, the majority of patients (9/11) received photodynamic pretreatment in combination with brachytherapy, and as many as 4 out of 11 patients died within 1 week after stent insertion as a result of esophageal wall rupture.

Table 3 Mean European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and EORTC QLQ-Oesophageal Module 18 (QLQ-OES18) scores (±standard deviation) at the inclusion and differences between scores at inclusion versus the follow ups

Time intervals	Inclusion (82%)†	1 mo (82%)†	2 mo (78%)†	3 mo (83%)†
EORTC QLQ-C30:				
Physical function‡	54 (±36)	−15	−10	−20
Role function‡	46 (±45)	−9	−7	−23
Emotional function‡	62 (±30)	−4	−8	−20
Cognitive function‡	76 (±28)	−5	−14	−3
Social function‡	65 (±34)	−4	−7	−30
Global quality of life‡	37 (±29)	−13	−7	−15
Fatigue§	55 (±33)	−10	−13	−18
Nausea or vomiting§	33 (±23)	−7	0	0
Pain§	35 (±28)	−13	−2	−7
Dyspnea§	19 (±24)	−4	−5	−7
Insomnia§	22 (±23)	0	−5	−13
Appetite loss§	82 (±16)	−7	−5	−7
Constipation§	51 (±47)	−4	+9	−7
Diarrhea§	12 (±24)	0	−5	0
Financial problems§	12 (±24)	−4	−5	0
EORTC QLQ-OES18:				
Dysphagia scale§	68 (±19)	+22	+17	+18
Eating scale§	61 (±28)	+8	+4	+8
Reflux scale§	12 (±17)	−9	−5	−7
Local pain scale§	23 (±21)	−7	0	−2
Trouble swallowing saliva§	43 (±29)	+15	+14	+13
Problems with choking§	27 (±36)	+11	+14	+7
Dry mouth§	29 (±20)	0	−5	−7
Problem with taste§	41 (±43)	−4	−9	−13
Trouble with coughing§	15 (±17)	+7	0	+7
Trouble with speech§	26 (±28)	−4	−5	0

†Answering frequency, mo = month. ‡A high score for functional scales and the global quality of life scale represents a high level of function. §A high score for a symptom scale or single item represents severe symptoms. A difference of 10 points or more was defined as a clinically relevant difference. +, improvement, –, deterioration.

Consequently, the authors draw the conclusion that stenting after pretreatment of the esophagus is a hazardous procedure. However, in the study by Yu *et al.* ($n = 10$), no major complications occurred; the treatment was well tolerated and survival ranged between 14 and 22 months. However, in the latter study, three fractions of low-dose (4 Gy) brachytherapy were applied, and homemade stents were used in the majority of patients. Furthermore, it is unclear which disease states the patients presented with, what grade of dysphagia relief was achieved, and how it affected HRQL.

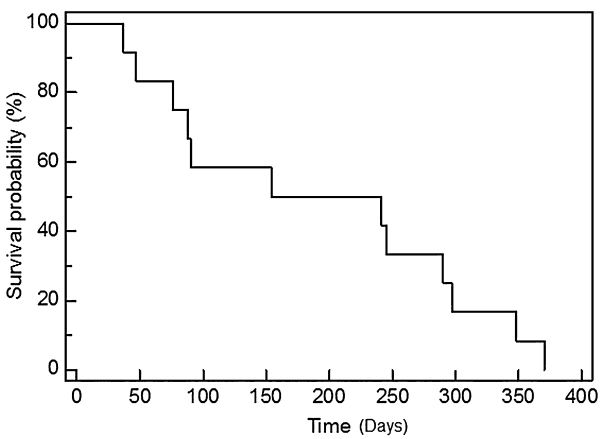

Fig. 2 Kaplan–Meier survival curve for patients included in the present study ($n = 12$).

Another interesting and recent study presents the results of conventional stent treatment compared with those achieved with stents loaded with Iridium[125] seeds.[21] In this randomized study incorporating 57 patients, the authors report more long-lasting relief of dysphagia and extended survival for the latter type of stent. The limited access to and potentially risky handling of radioactive stents, however, represent obstacles in performing this type of treatment. Conventional stents and intraluminal brachytherapy, on the other hand, already exist at most centers involved in the treatment of this patient group.

Optimally, combined stent insertion and brachytherapy can be performed simultaneously to reduce the number of interventions needed and to minimize the duration between the two stages of the procedure. A one-session strategy might even counteract the difficulties that we experienced with one patient in passing the guidewire through the previously deployed stent. However, there is a certain time lag for the stent to become fully expanded; another potential problem might be the dislocation of the stent by the brachytherapy applicator. Although no severe adverse event, such as massive bleeding or perforation, occurred in our series, it must be kept in mind that ours is a small pilot study. No conclusion may be drawn regarding this combined strategy's potential superiority compared with stent treatment or brachytherapy alone. The minor complications that arose, however, are well documented in most studies focusing on the various palliative regimes that are given to these patients.

The obvious sequel to this pilot study would be to set up a randomized trial comparing the pros and cons of the combination of stent insertion and brachytherapy to that of treatment with stent or brachytherapy alone. Such a trial would preferably be double blinded and could use the dysphagia score (according to Ogilvie *et al.*[10]) as primary endpoint. An alternative to the latter would be to use the dysphagia scale score, or possibly, the GQoL score of the EORTC QLQ-OES18 questionnaire.

In summary, our pilot study showed that combined stent and single high-dose brachytherapy in patients with advanced esophageal cancer can be administered in a safe and effective manner. This strategy seems to be applicable in most patients, regardless of the expected remaining lifespan, where palliation is the main goal. A randomized trial comparing the efficacy of this new strategy to that of stent insertion or brachytherapy alone is, therefore, warranted.

Acknowledgments

This study was supported by grants from the Assar Gabrielsson Foundation and the Gothenburg Medical Society. The authors declare no competing financial interests.

References

1 Talback M, Rosen M, Stenbeck M, Dickman P W. Cancer patient survival in Sweden at the beginning of the third millennium – predictions using period analysis. Cancer Causes Control 2004; 15: 967–76.
2 Tytgat G N, Bartelink H, Bernards R *et al*. Cancer of the esophagus and gastric cardia: recent advances. Dis Esophagus 2004; 17: 10–26.
3 Bergquist H, Wenger U, Johnsson E *et al*. Stent insertion or endoluminal brachytherapy as palliation of patients with advanced cancer of the esophagus and gastroesophageal junction. Results of a randomized, controlled clinical trial. Dis Esophagus 2005; 18: 131–9.
4 Homs M Y, Steyerberg E W, Eijkenboom W M *et al*. Single-dose brachytherapy versus metal stent placement for the palliation of dysphagia from oesophageal cancer: multicentre randomised trial. Lancet 2004; 364: 1497–504.
5 Wenger U, Johnsson E, Bergquist H *et al*. Health economic evaluation of stent or endoluminal brachytherapy as a palliative strategy in patients with incurable cancer of the oesophagus or gastro-oesophageal junction: results of a randomized clinical trial. Eur J Gastroenterol Hepatol 2005; 17: 1369–77.
6 Sreedharan A, Harris K, Crellin A, Forman D, Everett S M. Interventions for dysphagia in oesophageal cancer. Cochrane Database Syst Rev 2009; (4): CD005048.
7 Steyerberg E W, Homs M Y, Stokvis A, Essink-Bot M L, Siersema P D. Stent placement or brachytherapy for palliation of dysphagia from esophageal cancer: a prognostic model to guide treatment selection. Gastrointest Endosc 2005; 62: 333–40.
8 Bergquist H, Johnsson A, Hammerlid E, Wenger U, Lundell L, Ruth M. Factors predicting survival in patients with advanced oesophageal cancer: a prospective multicentre evaluation. Aliment Pharmacol Ther 2008; 27: 385–95.
9 Liedman B L, Bennegard K, Olbe L C, Lundell L R. Predictors of postoperative morbidity and mortality after surgery for gastro-oesophageal carcinomas. Eur J Surg 1995; 161: 173–80.
10 Ogilvie A L, Dronfield M W, Ferguson R, Atkinson M. Palliative intubation of oesophagogastric neoplasms at fibreoptic endoscopy. Gut 1982; 23: 1060–7.
11 Siersema P D, Marcon N, Vakil N. Metal stents for tumors of the distal esophagus and gastric cardia. Endoscopy 2003; 35: 79–85.
12 Schag C C, Heinrich R L, Ganz P A. Karnofsky performance status revisited: reliability, validity, and guidelines. J Clin Oncol 1984; 2: 187–93.
13 Aaronson N K, Ahmedzai S, Bergman B *et al*. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993; 85: 365–76.
14 Fayers P M, Aaronson N K, Bjordal K, Curran D, Groenvold M. EORTC QLQ-C30 Scoring Manual. Brussels: EORTC, 1997.
15 King M T. The interpretation of scores from the EORTC quality of life questionnaire QLQ-C30. Qual Life Res 1996; 5: 555–67.
16 Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 1998; 16: 139–44.
17 Blazeby J M, Conroy T, Hammerlid E *et al*. Clinical and psychometric validation of an EORTC questionnaire module, the EORTC QLQ-OES18, to assess quality of life in patients with oesophageal cancer. Eur J Cancer 2003; 39: 1384–94.
18 Good P. Permutation Tests. A Practical Guide to Resampling Methods for Testing Hypotheses. New York: Springer, Inc, 2000.
19 Maier A, Pinter H, Friehs G B, Renner H, Smolle-Juttner F M. Self-expandable coated stent after intraluminal treatment of esophageal cancer: a risky procedure? Ann Thorac Surg 1999; 67: 781–4.
20 Yu Y T, Yang G, Liu Y, Shen B Z. Clinical evaluation of radiotherapy for advanced esophageal cancer after metallic stent placement. World J Gastroenterol 2004; 10: 2145–6.
21 Guo J H, Teng G J, Zhu G Y *et al*. Self-expandable esophageal stent loaded with 125I seeds: initial experience in patients with advanced esophageal cancer. Radiology 2008; 247: 574–81.