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ORIGINAL ARTICLE

External beam radiotherapy versus brachytherapy in the management of malignant oesophageal dysphagia: a retrospective study

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Summary

Purpose: *Dysphagia is a prominent symptom of oesophageal cancer which may be palliated by stent, external beam radiation (EBRT) or intraluminal brachytherapy (ILBT). Brachytherapy is not widely practised in the UK. The aim of this study was to compare the efficacy of ILBT and EBRT in relieving malignant dysphagia.*

Methods: *The radiotherapy database at Northampton Cancer Centre (NCC) was used to identify patients who underwent ILBT or EBRT for malignant dysphagia between 1.1.2008 and 31.3 2010. Data was collected on patient demographics, tumour characteristics, treatment received and dysphagia score pre- and post- treatment. Serial assessment of dysphagia was used to determine the duration of symptomatic improvement. EBRT involved 20-30 Gy in 5-10 fractions. Brachytherapy applicator placement was done by an experienced endoscopist at the high dose rate (HDR) suite and a single treatment dose of 12 Gy was prescribed at 1 cm depth. Oesophageal dilation was performed prior to brachytherapy treatment if needed.*

Results: *44 patients were included in this study (EBRT: 21; ILBT: 23). Patient characteristics were well balanced between the two groups. The average dysphagia scores in the EBRT group prior to treatment were 3, and at 4, 8 and 16 weeks following treatment they were 3.4, 2.4, 2.1 and 2.1, respectively. The corresponding dysphagia scores in the ILBT group were 3.5 before treatment and 2.2, 2.1 and 2.3 following treatment, respectively. There was significant improvement in dysphagia in both groups at 4 weeks ($p<0.0001$), and the benefit was sustained after 8 and 16 weeks. No major complications were reported from either EBRT or oesophageal brachytherapy.*

Conclusion: *ILBT is an effective alternative to multifractionated EBRT for palliation of malignant dysphagia providing a convenient one-stop treatment for patients who live a long distance from their cancer centre. Our model of performing the endoscopically guided procedure in the brachytherapy unit is comparable in cost to fractionated EBRT and can be adopted by other centres.*

Key words: brachytherapy, external beam radiotherapy, malignant dysphagia

Introduction

Of about 400 000 patients who are diagnosed with oesophageal cancer worldwide each year, more than 350 000 die from this disease, with an overall 5-year survival rate of 10-15% [1]. Its incidence has risen significantly over the past two decades in the developed world, primarily because of rise in the incidence of adenocarcinoma of the lower oesophagus and gastro-oesophageal junction. About 80% of patients have inoperable disease and most of these patients need palliative treatment to relieve symptoms of progressive dysphagia.

The commonly used treatment options for palliation of malignant dysphagia include self expanding metal stent (SEMS), EBRT and ILBT [2]. In the UK, there is variation in the procedures used to palliate dysphagia depending on local expertise but ILBT is not widely practised. Randomised data indicate superior outcome from ILBT compared to SEMS for long-term relief of dysphagia and Health Related Quality of Life (HRQL) [3,4] but there are no comparative studies evaluating the efficacy and morbidity of ILBT vs. EBRT. We therefore retrospectively reviewed the outcome of patients undergoing either modality in our hospital over a 2-year period.

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Methods

The radiotherapy database of Northampton Cancer Centre was used to identify patients who underwent ILBT or EBRT for malignant dysphagia from oesophageal cancer between 01.01.2008 and 31.3.2010. Individual paper notes and the Oncology Database (an electronic database holding clinical records of all patients undergoing oncology treatment at NCC) were reviewed and data was collected on patient demographics, tumour characteristics, treatment received and dysphagia score pre- and post-treatment. The modified O'Rourke Swallowing Function Scoring System was used to score dysphagia [5]. Patients underwent 4-weekly follow-up visits in the initial 3-4 months following their treatment. Dysphagia score was recorded prospectively at each follow-up which allowed serial assessment of dysphagia to determine the duration of symptomatic improvement.

EBRT involved 20-30 Gy radiation in 5-10 fractions delivered over 1-2 weeks using parallel opposed anterior-posterior beams and megavoltage photons (6-10 MV). All patients receiving EBRT underwent CT simulation and the treatment fields were defined incorporating information from diagnostic imaging and endoscopy reports.

ILBT was delivered as a one-stop procedure where a single experienced gastroenterologist performed a preliminary upper gastrointestinal endoscopy and dilatation of the stricture if necessary. A 6 mm oesophageal applicator (Nucleotron®) was then placed under endoscopic guidance. Using radioactive ^{192}Iridium source, a single treatment dose of 12 Gy was prescribed at 1 cm from the active dwell positions, using equal dwell times to reduce dosimetric hotspots. The treatment length included the tumour with a margin of 2 cm in the superior and inferior direction.

Statistical considerations

Overall survival (OS) was calculated according to the Kaplan-Meier method. OS was defined as the time from the date of initial diagnosis until death from any cause. All events were measured from the last day of therapy.

Statistical methods: mean, median, standard deviation and frequency were used to describe data. Life tables, log rank test, Cox regression and hazard ratio were used to test the effect of different risk factors on survival. A p value was considered statistically significant if less than 0.05. Tests were run on an IBM compatible PC using an SPSS for windows statistical package, version 17 (SPSS Inc., Chicago, IL).

Results

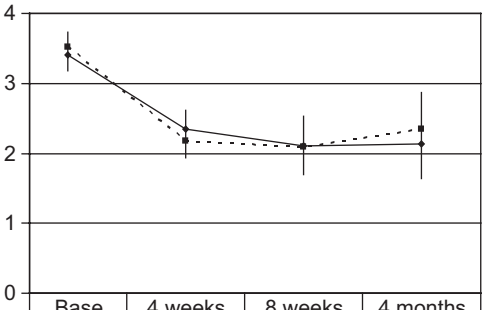
Forty-four patients were included in this study (EBRT: 21; ILBT: 23). Patient and tumour characteristics were well balanced between the two groups although there was a higher proportion of patients with adenocarcinoma in the ILBT group which approached statistical significance (p=0.09; Table 1). Five patients received both treatments (EBRT, then brachytherapy at recurrence of dysphagia or *vice versa*) and were included in both groups. Six patients in the EBRT group and 5 patients in the ILBT group also received chemotherapy. One patient in the EBRT group had prior radical surgery.

Table 1. Patient and tumour characteristics

Characteristics	*EBRT*	*ILBT*	*p-value*
Patients, N	21	23	
Mean age, years (range)	71 (51-89)	72 (41-92)	0.95
Sex			0.30
Male	15	18	
Female	6	5	
Histology			0.09
Adenocarcinoma	8	16	
Squamous cell carcinoma	11	6	
Other	2	1	
Baseline dysphagia score	3.4	3.5	0.54

EBRT: external beam radiotherapy, ILBT: intraluminal brachytherapy

The mean dysphagia scores in the EBRT group prior to treatment were 3, and at 4, 8 and 16 weeks following treatment they were 3.4, 2.4, 2.1 and 2.1, respectively (Figure 1). The corresponding dysphagia scores in the ILBT group were 3.5 before treatment and 2.2, 2.1 and 2.3, following treatment, respectively. There was significant improvement in dysphagia in both groups at 4 weeks ($p<0.0001$), and the benefit was sustained after 8 and 16 weeks. There was no statistical difference between the EBRT and ILBT groups with regard to dysphagia improvement or survival, and the histological subtype did not influence response. Two (9%) patients in the EBRT group and 4 (17%) in the ILBT group did not benefit from radiotherapy (p=0.85). Within the follow-up period stent placement was required in 5 (24%) patients in the EBRT group and in 3 (13%) in the ILBT group (p=0.07). The follow-up after 4 months was unreliable as many of the patients died or underwent follow-up in Milton Keynes and Kettering General Hospital or in hospices. There was no difference in OS between the two groups (log rank, p=0.84).



	Base	4 weeks	8 weeks	4 months
95%	3.62	2.61	2.53	2.64
Mean Group 1	3.4	2.35	2.11	2.14
-95%	3.18	2.09	1.69	1.64
95%	3.73	2.4	2.44	2.87
Mean Group 2	3.52	2.17	2.09	2.35
-95%	3.31	1.94	1.74	1.83

Figure 1. Graph showing improvement in dysphagia grade in the two groups. Group 1: external beam RT. Group 2: intraluminal brachytherapy.

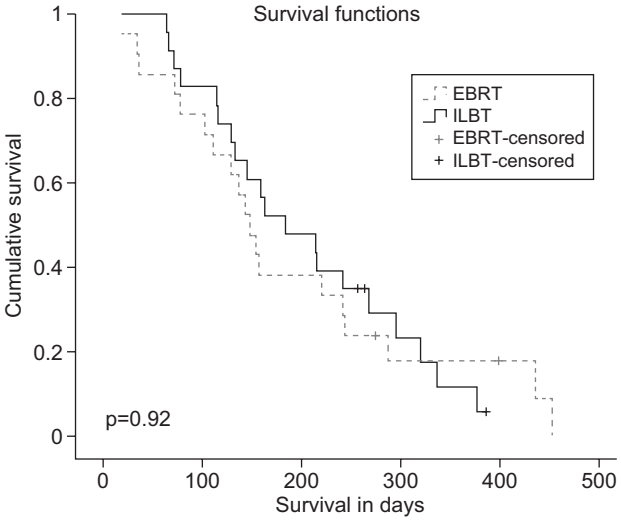


Figure 2. Survival graph showing survival difference between the two groups. EBRT: external beam RT, ILBT: intraluminal brachytherapy.

The median OS for the EBRT group was 148 days and for the ILBT 184 days (p=0.92; Figure 2).

No major complications or side effects were reported from ILBT or EBRT.

Discussion

This study evaluated a selected patient population who were not suitable for radical therapy. Despite the small number of patients, to the best of our knowledge this represents the only series reporting experience of ILBT from the UK [6].

Although SEMS is more widely used in the UK, ILBT is a suitable alternative to SEMS in the management of malignant dysphagia and provides more durable symptom relief and improved quality of life. Two randomised studies have compared SEMS with ILBT. In the study by Bergquist et al. 65 patients with advanced oesophageal and gastro-oesophageal cancer were randomised to ILBT or SEMS [3]. The latter provided a more instant relief of dysphagia, but 3-month dysphagia scores and HRQL scores were significantly better in the brachytherapy arm. Homs et al. randomised 209 patients to SEMS or single dose 12 Gy ILBT [4]. Although dysphagia improved more rapidly after SEMS, long term relief of dysphagia and quality of life scores favoured brachytherapy, and stent placement led to more complications (33 vs. 21%, p=0.02). A 10-year retrospective review by Homs et al. evaluated the functional outcome, complications, recurrent dysphagia and survival in 149 patients treated with ILBT at a median dose of 15 Gy [6]. There was a significant improvement in median dysphagia score from 3 to 2 ($p<0.001$); early and late procedure-related complications were reported in only 5% and 7% of the patients, respectively. Of the 104 patients where both baseline and 6-week follow-up dysphagia scores were available, 51% of the patients demonstrated improvement in dysphagia scores; 37% experienced recurrent dysphagia after a median time period of 3 months and in 23% a metal stent was placed to relieve persistent or recurrent dysphagia. In a more recent study by Frobe et al. ILBT was delivered as 2 doses of 8 Gy each, one week apart, in patients with squamous cell carcinoma (n=29) [7]. Over a 4-month follow-up, quality of life was statistically improved with regards to feelings ($p= 0.013$), sleeping ($p=0.032$), eating ($p=0.020$), and social life ($p=0.002$). Dysphagia was significantly improved ($p < 0.006$) with a dysphagia score reduction of 0.52 units from baseline. Fabrini et al. reported their brachytherapy experience in 104 patients, 53 of whom received ILBT with palliative intent [8]. Dysphagia was controlled in 84.6% of them with a low rate of severe complications. In our own experience, 83% (19/23) of the patients receiving ILBT achieved symptom relief and none encountered severe treatment-related complications - this outcome is similar to that reported by Fabrini et al. and superior to that reported by Homs et al. [6], most likely due to careful patient selection as most of our patients with grade 4-5 dysphagia would have been referred for SEMS.

In appropriately selected patients both ILBT and EBRT have been reported as effective treatments for relieving malignant dysphagia. However, there are no studies that have directly compared the efficacy of EBRT against ILBT - although retrospective in nature, this is the first study that attempts such a comparison and reports very similar outcome. Interestingly, one randomised controlled trial has demonstrated that combining EBRT with ILBT was superior to ILBT alone in improving dysphagia ($p=0.00005$), chest pain ($p=0.0038$), odynophagia ($p=0.006$), regurgitation ($p=0.00005$) and performance status ($p=0.0015$), suggesting the use of this combination can maximize local control [9]. A similar combination of intraluminal intervention ± EBRT will be evaluated in the UK in the ROCS trial (CI: Douglas Adamson and Anthony Bryne; contact Lisette Nixon: WMDLSN1@wctu.cf.ac.uk) which proposes to randomise 396 patients between SEMS with/without EBRT (20-30 Gy in 5-10 fractions).

Our study suggests that patients could be offered a choice between either modalities without loss of efficacy or risk of additional toxicity. For patients living a long way from the cancer centre, ILBT is an attractive option providing a one-stop treatment. Conversely, patients with bulky tumour and symptomatic locoregional

disease are more likely to benefit from EBRT alone or in combination with ILBT.

EBRT is simple to co-ordinate and non-invasive. It is therefore very tempting to embrace this as the sole radiotherapy option in any institution. However, if the logistics of co-ordinating endoscopist's and oncologist's time and availability of HDR suite and radiotherapy staff can be overcome, ILBT provides a convenient one-stop alternative for patients who are relatively frail and who may find the travel for a fractionated course EBRT rather onerous.

Limitations of this study

As with all retrospective studies, there is a likelihood of bias in selecting patients for either modality. Patients with severe dysphagia (grade 4-5) were likely to have been referred for SEMS, whereas less severe cases would have been offered the choice of SEMS or radiotherapy. The treatment choice between EBRT and ILBT may have been influenced by factors such as tumour bulk, patient preference, urgency to treat (ILBT is available on alternate Tuesdays only) and presence or absence of other symptoms/ such as pain or local-regional lymphadenopathy. This was not clearly assessable from the patients' notes; however, the baseline dysphagia scores were comparable and would support the notion that the magnitude of benefit from either modality was comparable.

Conclusion

Brachytherapy is an effective alternative to multifractionated EBRT for palliation of malignant dysphagia, providing a convenient one-stop solution for patients who live a long distance from their cancer centre. Our model of performing the endoscopically guided procedure in the brachytherapy unit is cheaper in cost compared to fractionated EBRT and can be adopted by other centres. We recommend a prospective randomised study of brachytherapy vs. EBRT evaluating efficacy, complication rate, quality of life and patient preference to help defining the role of either modality in this group of patients.

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