Palliative radiotherapy combined with stent insertion to reduce recurrent dysphagia in oesophageal cancer patients: the ROCS RCT

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Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

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Scientific summary

The ROCS RCT

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Scientific summary

Background

The majority of oesophageal cancers occur in those aged ≥ 60 years. Most patients have advanced disease at presentation, with an average survival of 3–5 months.

The focus of treatment is frequently on effective palliation, with many patients requiring intervention for dysphagia. This single symptom has a profound impact on social and physical functioning and other aspects of quality of life. Interventions to improve swallowing should aim to produce prompt and lasting palliation while minimising the impact that the intervention has on other aspects of quality of life, as well as reducing the need for late reinterventions and hospitalisation towards the end of life.

Systematic reviews have shown that the insertion of self-expanding metal stents is the quickest way to restore the ability to swallow in severe dysphagia but patients who have a stent suffer from issues with pain, poorer quality of life and recurrence of dysphagia in the 2–3 months prior to death. These reviews have called for randomised trials of interventions combined with stents to address these problems, and for such studies to include a robust assessment of quality of life and cost-effectiveness.

External beam radiotherapy is widely accessible to patients with advanced cancer and is frequently used to palliate symptoms. By contrast, brachytherapy accounts for < 2% of palliative interventions in this context in the UK. External beam radiotherapy may, therefore, represent an appropriate intervention alongside stenting to maintain swallow and reduce symptom burden.

Objectives

The main objective of the study was to assess whether or not the addition of external beam radiotherapy reduces the risk of recurrent dysphagia in oesophageal cancer patients receiving insertion of a stent as the primary treatment. We also wanted to assess the impact that insertion of a stent has on other aspects of quality of life and bleeding risk as well as assessing the cost-effectiveness of adding external beam radiotherapy at the time of stent insertion. An embedded qualitative study explored patient experience in relation to:

- trial involvement and study processes
- acceptability of the intervention and perceived trade-offs of burdens and benefits
- experiences of having a stent inserted and living with advanced oesophageal cancer.

Methods

We conducted a pragmatic, multicentre, randomised controlled trial comparing usual stent placement with usual stent placement followed by palliative external beam radiotherapy at a dose of 20 Gy in five fractions or, at clinician discretion, 30 Gy in 10 fractions. The randomisation ratio was 1 : 1 and was stratified by centre, stage at diagnosis (I–III vs. IV), histology (squamous or other) and multidisciplinary team intent to give chemotherapy (yes or no).

Participants were patients (and their carers for the qualitative study) with incurable oesophageal carcinoma referred for a stent as palliation of dysphagia. They were recruited from 23 sites across the UK and referred by members of the local upper gastrointestinal multidisciplinary team.

The inclusion criteria were age ≥ 16 years, being referred for a stent as primary treatment of dysphagia, being unsuitable for radical treatment, having an expected survival of at least 12 weeks and being deemed clinically able to tolerate radiotherapy, having the ability to provide written informed consent, and having completed, as a minimum, the baseline dysphagia questionnaire.

The primary outcome was recurrent dysphagia, or death, at 12 weeks. Dysphagia was defined as an 11-point deterioration in the European Organisation of Research and Treatment of Cancer-OG25 dysphagia score (or a dysphagia-related event consistent with such a deterioration). To detect a reduction in this proportion from 40% to 20% required 164 participants (80% power, 5% alpha two-sided), or 220 participants allowing for 25% loss to follow-up. Secondary outcomes included other key health-related quality-of-life outcomes, bleeding events and cost-effectiveness. Patients were followed up 4-weekly for 12 months, with additional 2-weekly in-between telephone calls to determine dysphagia scores.

All follow-up assessments were planned to take place at home to minimise patient burden. Investment in additional research nurse time and training was implemented to achieve this and to maximise data capture. A subgroup of patients and their carers contributed to the in-depth qualitative interviews that were analysed by thematic analysis.

Results

A total of 220 patients were randomised over 4.6 years. Eligibility was 43.6%, with a consent rate of 40%. Of those randomised, 112 were allocated to the usual-care arm and 108 were randomised to the external beam radiotherapy arm. Twenty-one patients were excluded from the modified intention-to-treat population (no stent inserted or no baseline dysphagia score), leaving 102 in the usual-care arm and 97 in the external beam radiotherapy arm. Baseline characteristics were comparable between arms. Assessment of adherence to radiotherapy showed that 15 out of 97 (15.4%) evaluable patients either died or withdrew prior to radiotherapy. Data returns were very good up to week 12 (149 with complete data sets to week 12) but reduced significantly after 12 weeks.

The primary analysis demonstrated that the addition of radiotherapy did not reduce the proportion of primary events at 12 weeks (48.6% in the usual-care arm vs. 45.3% in the external beam radiotherapy arm; adjusted odds ratio 0.82, 95% confidence interval 0.40 to 1.68; $p = 0.587$) and that it was less cost-effective to this point. Sensitivity analyses did not alter the results. Dysphagia deterioration-free survival was similar in both arms and median survival was 19.7 weeks in the usual-care arm and 18.9 weeks in the external beam radiotherapy arm.

Those in the radiotherapy arm had significantly fewer bleeding events. Up to week 16, in the usual-care arm 18.6% of patients had a bleeding related event, compared with 10.3% in the external beam radiotherapy arm, giving a number needed to treat of 12. The effect persisted and increased over time, and by 52 weeks 28.4% in the usual-care arm, compared with 16.5% in the radiotherapy arm, had an event, giving a number needed to treat of eight.

Key secondary health-related quality-of-life outcomes were not different, but initial fatigue and pain scores tended to be higher in the radiotherapy arm, and were recorded more often as significant toxicities.

Qualitative enquiry indicated that some patients in the radiotherapy arm found the intervention tiring and burdensome to attend. In the qualitative interviews, patients in both arms also described significant challenges with eating restrictions and worries about nutrition. They adopted trial-and-error approaches to daily life and sought to reframe their hope in relation to better quality of life rather than survival.

Implications for health care

- We can conclude that patients with advanced oesophageal cancer requiring a self-expanding metal stent to improve dysphagia will not benefit further from the addition of concurrent palliative external beam radiotherapy, and are likely to find the trade-offs of fatigue and additional hospital visits too burdensome. For those who have a longer prognosis and are considered to have an increased risk of tumour bleeding, concurrent external beam radiotherapy may reduce bleeding risk and associated interventions. However, when offering patients this intervention, information about the impact on quality of life and trade-offs will be important to inform decision-making.
- Insertion of a stent for dysphagia does not address the experience of patients in relation to eating concerns, symptoms and adapting to uncertainty. Patients and carers required timely and ongoing support from multidisciplinary professionals with the important psychosocial and physical aspects of nutrition and eating. They also require help in negotiating uncertainty and the reframing of hope towards quality of life rather than survival.

Implications for future research

- Future studies will be important to define other interventions that may usefully be combined with self-expanding metal stent to improve swallow outcomes. Such studies may benefit from insights gained during the Radiotherapy after Oesophageal Cancer Stenting (ROCS) study on trial conduct in this context. Investing in additional research practitioner time and training that allows follow-up data collection at home, timing of randomisation after stent insertion to allow more time for patient identification and trial consideration, and regular meetings of the multisite research practitioners to share best practice can all improve trial conduct. Embedded qualitative methods can also ensure that intervention combinations are properly assessed in terms of patient experience and perceptions of trade-offs between treatment benefits and burdens.
- The ROCS study has highlighted significant unmet supportive and palliative care needs of patients with advanced oesophageal cancer, including multifaceted aspects of eating and nutrition. Further research is required to define the most effective elements of multidisciplinary supportive interventions, specifically in relation to the multidimensional concerns around eating and nutritional intake, and the triggers for timely multiprofessional involvement.

Trial registration

This trial is registered as ISRCTN12376468 and Clinicaltrials.gov NCT01915693.

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This report

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