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Swallowing beyond six years post (chemo)radiotherapy for head and neck cancer; a cohort study

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ABSTRACT

Objective: The objective of this prospective study is to report on long-term swallowing outcomes in a group of head and neck cancer patients following (chemo) radiotherapy treatment, assess for changes over time and identify any predictor variables of outcome.

Materials and methods: 42 survivors were assessed on four swallowing measures and followed up from pre-treatment to six years post 3D (chemo) radiotherapy. Measures included a swallowing specific QOL questionnaire, penetration-aspiration scale, dietary restrictions and a timed water swallow test.

Results: At six years, 71% reported swallowing difficulties on the questionnaire. One fifth of patients had aspiration, with a raised risk of chest infection. Seven percent required a laryngectomy for a dysfunctional larynx. Despite this, half the group reported having a normal diet. There was variation in the pattern of change between one and six years. A significant deterioration was only observed in the timed water swallow test ($p < 0.0001$). Larger radiotherapy volume predicted this outcome. None of the variables tested predicted outcome for the other three swallow measures.

Conclusion: Patients continue to report swallowing difficulties at six years, with a proportion having persistent aspiration. Further work on identifying the risk factors associated with aspiration tolerance, aspiration pneumonia, prevention and management is warranted. Long-term dysphagia remains a significant and serious concern following (chemo) radiotherapy for HNC and swallowing outcomes should continue to be monitored over time.

Introduction

Dysphagia is a common and serious side effect of chemoradiotherapy (CRT) for head and neck cancer (HNC). A small number of longitudinal studies describe swallowing outcomes with follow up periods ranging from six to 24 months. These report on patients following Intensity Modulated CRT [1,2], or accelerated radiotherapy for pharyngeal cancer [3], or a combination of post-radiotherapy and post-CRT patients [4,5]. All identify a significant deterioration in swallowing from pre- to post-treatment. There is disagreement about the subsequent trajectory, three reporting little recovery up to two years following treatment [1,3,4], whereas others [2,5] report some improvement, but without a return to pre-treatment status. Little information is available on long-term swallowing outcomes beyond two years with conservative prevalence estimates of dysphagia being between 50 and 60% of HNC survivors [6]. A small number of case series and cross-sectional data report late onset dysphagia and high rates of aspiration-related deaths [7–9]. Other authors estimate the incidence of aspiration pneumonia as being 24% up to five years post CRT, with over 80% of these cases needing to be hospitalised, half of whom subsequently required transfer to intensive care [10]. A prospective five year follow up study reported good dysphagia-specific questionnaire outcomes, but a decline in swallowing efficiency over time [11].

Our published longitudinal study recorded swallowing outcomes in a consecutively recruited sample, from pre-treatment up to one year post 3D conformal CRT [12]. There was marked deterioration on all swallowing measurements from pre to post-treatment. Aspiration occurred in up to 28% of patients. Half of them were able to manage at best, a soft chewable diet, and 72% reported swallowing difficulties on a dysphagia-specific questionnaire. Improvement in the first year occurred on some clinical measures, but limited change was observed in patients' perceptions of swallowing function and quality of life. Pre-treatment swallowing status was predictive of outcomes at one year, across all measures, with radiotherapy treatment volume predicting

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dietary restrictions and swallow capacity. The current longitudinal follow-up study reports on the prevalence of long-term swallowing difficulties in this same cohort of HNC patients up to six years following CRT, compares outcomes with one year data and explores factors that predict outcome in the long-term.

Patients and methods

This investigation is a long-term prospective cohort study of all disease free patients at six years post-(C)RT, who participated in our previous one-year swallow outcome study [12,13].

Patients

HNC patients treated by radiotherapy +/− chemotherapy, with curative intent were prospectively and consecutively recruited in 2005–2007 from two hospitals in North East England. Patients were excluded if their primary disease had been treated with surgery; they had recurrent/residual disease or if they reported pre-existing dysphagia. The radiotherapy regime was 63 Gy in 30 fractions over six weeks using 3D conformal techniques. Patient treated with CRT had radiotherapy, combined with either Cisplatin 40 mg/m^2 in six cycles or Mitomycin C 15 mg/m^2 in two cycles. Treatment volume ranged from 240 to 2226 cc. Data for the initial study [12,13] were collected at four time points: pre-treatment, three, six and twelve months post-treatment. At six years, hospital databases were checked for survival status and whether the patient still resided in the area. Surviving patients were contacted, including those previously lost to follow up, and invited for a swallowing assessment follow-up. Prophylactic swallowing exercises were not given pre-treatment, but all patients were offered post-treatment swallowing rehabilitation as part of standard care at both centres. The long-term study was approved by Sunderland (UK) local ethics research committee. All patients gave written consent.

Swallowing outcomes

The same four dimensions of swallowing were assessed as previously described [12].

1. Patient rated swallowing outcomes were collected using the MD Anderson Dysphagia Inventory (MDADI [14]), a swallowing-related quality of life questionnaire. A difference of ten points indicates a clinically important difference [15].
2. Fiberoptic Endoscopic Evaluation of Swallowing (FEES) using a Pentax 3.2 mm flexible nasendoscope and digital recording. Patients drank 10 mLs of blue dyed milk and were rated by a speech & language pathologist, using Rosenbek's Penetration-Aspiration scale [16]. Twenty percent of the clips were re-rated at least two months after the initial examination to test for intra-rater reliability. Ten percent of recordings were rated by a second assessor, who was blinded to the patient's details and the initial score, to assess for inter-rater reliability.
3. Patients' dietary restrictions were rated using the Normalcy of Diet (NoD) scale which is a sub-section of the Performance Status Scales [17].
4. Swallow performance was assessed using the timed 100 mL Water swallow test (WST [18]). From this, a measure of swallow capacity (mLs per second) was calculated. The test was not performed if the patient reported choking on fluids and in these circumstances was scored as a zero. Preliminary work indicates that a difference of seven mLs/sec represents a clinically important difference [19].

In addition, patients were asked if they had had a chest infection requiring antibiotics over the previous year.

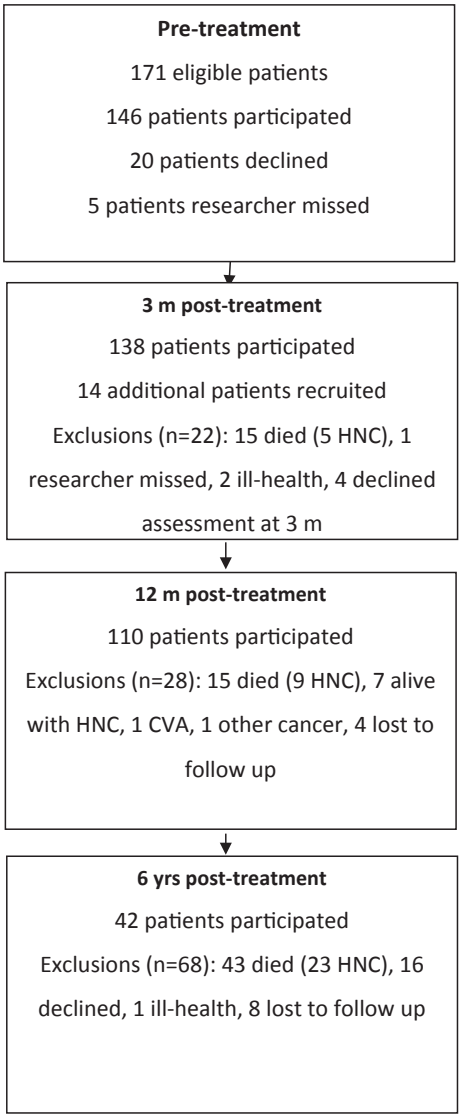

Fig. 1. Recruitment and retention of patients for the total sample.

Statistical analysis

Data were analysed using SPSS version 20. Paired t-tests or, Mann Whitney tests (depending on data distribution) and Pearson's Chi squared test were used to compare one and six year continuous and categorical data respectively. No imputation techniques were employed to adjust for missing data. Patients with oropharynx cancer represented the largest tumor site and descriptive statistics are presented for this sub-group, in addition to the total group. To test potential predictors of long-term outcome, multiple regression models were constructed using the end point measure (6 year swallowing outcomes), as the dependent variable. All 4 measures of dysphagia were analysed in separate regression models. Treatment volume, patient demographics (age and sex), and the equivalent pretreatment swallowing score were entered as independent variables for each of the four models as per our previous study. Tumor site was not included as a variable, due to the small numbers in some sub-groups. Forced entry regression was used as no assumptions could be made about the ranking of the independent variables in the models.