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Original article

Long term patient reported swallowing function following chemoradiotherapy for oropharyngeal carcinoma

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ABSTRACT

Background and purpose: Limited data are available to inform on long term swallowing outcomes following concurrent chemoradiotherapy for oropharyngeal carcinoma. The aims of this study are to determine long term patient-reported swallowing outcomes across two large UK centres in routine clinical practice and identify associated factors.

Material and methods: All patients treated for oropharyngeal squamous cell carcinoma with concurrent chemoradiotherapy, and irradiation of the bilateral neck, between 2011 and 2013 were identified. Those requiring therapeutic enteral feeding prior to treatment, or having subsequent disease relapse, were excluded from the study. Patients were sent postal invitations to complete the MD Anderson Dysphagia Inventory (MDADI), at least two years following completion of treatment.

Results: Completed MDADI were received from 201/242 eligible patients (83%) at a median of 3.4 years (range 2–5) post treatment. Median composite MDADI score was 68.4. 64 (32%) had composite MDADI <60 classed as 'poor' function, 76 (38%) scores ≥60–<80 classed as adequate function, and 61 (31%) had scores ≥80 classed as optimal function. Patients with normal and abnormal pre-treatment diet had median composite MDADI scores of 70.5 versus 47.4 respectively. Patients who did not require enteral feeding during treatment and those who did had median composite MDADI scores of 76.3 versus 65.3 respectively. On multivariate analysis poorer performance status, abnormal pre-treatment diet, and use of enteral feeding during radiotherapy were all significantly associated with lower composite, global and subscale MDADI scores.

Conclusions: Patient reported swallowing dysfunction remains common in the long term post-chemoradiotherapy. Impaired pre-treatment diet and use of enteral feeding during treatment are key factors associated with poorer swallowing outcomes.

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Intensity-modulated radiotherapy and concurrent chemotherapy is a standard of care for patients with locally advanced squamous cell oropharyngeal cancers. Although this achieves favourable disease outcomes, there is potential significant toxicity from treatment, which can adversely affect quality of life [1]. Multiple phases of swallowing mechanism can be affected by chemoradiotherapy [2]. Long term dysphagia is well recognised as a significant late toxicity following chemoradiotherapy, with some patients requiring long term enteral nutrition [3,4,5,6]. Several studies have demonstrated that this negatively impacts upon health-related quality of life [7,8]. A recent study showed at one year post treatment, dysphagia is a priority concern for patients [3]. Long term survivorship issues are particularly important for oropharyngeal carcinoma, with many patients having a favourable prognosis [9].

Dysphagia can be assessed by multiple methods, including physician-rated toxicity scores, objective physical measures such as videofluoroscopy, and patient reported measures [2]. Studies have shown that these outcome measures do not necessarily correlate, with patients rating dysphagia more severely [10,11,12,13]. Therefore, patient-reported outcome measures are particularly important in the assessment of swallowing function. The MD Anderson Dysphagia Inventory (MDADI) is a well-documented and validated patient-reported questionnaire to measure patients' perception of swallowing function and associated quality of life [14].

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Prior studies have demonstrated a temporal change in MDADI score, with scores reducing from baseline during treatment, with gradual improvement but remaining depressed compared with baseline 1–2 years post-treatment [3,15,16]. There are limited data on long term patient reported swallowing function following chemoradiotherapy, with most studies reporting outcomes less than 2 years following treatment [3,15,16]. A few studies have reported longer term outcomes in relatively small cohorts of patients [10,17,18].

We have previously reported long term patient reported swallowing outcomes in a small single centre cohort of 49 patients with oropharyngeal carcinoma treated between January 2011 and December 2012 with intensity modulated radiotherapy (IMRT) and concurrent chemotherapy who completed the MDADI more than 2 years post treatment [19]. Our aim was to extend this study in two large UK centres to determine long term patient reported swallowing outcomes using the MDADI following chemoradiotherapy for oropharyngeal carcinoma and to identify factors predictive of swallowing outcomes. This analysis describes outcomes in routine clinical practice, compared to the selected patient populations which may be represented within clinical trials.

Material and methods

Patient selection

The study was registered with the relevant Institutional Quality Improvement boards. This was an analysis of long term patient reported swallowing function, assessed using the MDADI questionnaire at least 2 years post treatment, in a consecutive series of patients who had been treated with concurrent chemoradiotherapy for oropharyngeal carcinoma in two large cancer centres (The Christie Hospital, Manchester, UK, and Leeds Cancer Centre, UK).

Consecutive patients were identified from electronic records treated in each centre between January 2011 and December 2013. Inclusion criteria were: oropharyngeal primary tumour, squamous cell histology, definitive non-surgical treatment delivered with curative intent, use of intensity modulated radiotherapy (IMRT), radiotherapy target including bilateral neck, concurrent platinum chemotherapy, disease free at time of study (at least 2 years from final day of radiotherapy). Exclusion criteria were: requiring therapeutic enteral feeding prior to radiotherapy, treatment given for recurrent disease or second primary tumour, known recurrence at the time of study, radiotherapy to the unilateral neck only.

Patients included in the study were sent postal invitations to complete an MDADI [14]. The initial cohort of 49 patients treated in Leeds between January 2011 and December 2012 had completed the postal MDADI questionnaire in 2015 (all >2 years post treatment) as previously reported and were included within this analysis [19]. The MDADI was posted in January 2017 to all patients treated at the Christie Hospital (130 patients), and all patients treated in Leeds during 2013 (49 patients).

The MDADI consists of 20 questions, which are scored on a five-point scale, ranging from 'strongly agree' to 'strongly disagree'. The MDADI is divided into emotional, function and physical subscales and two summary scores are obtained; the global scale is a single question scored individually and the composite is a score summarising the remaining 19 questions. The global score is one overarching question, while for the other subscales the answers are summed, and mean scores are multiplied by 20 to give an overall score within the range of 20–100, with higher scores indicating better swallowing function and quality of life. A further MDADI was sent out to non-responders after one to three months.

Patient records were reviewed to determine demographic information. Patients were staged according to TNM 7th Edition [20]. Pre-treatment diet was determined from contemporaneous dietetic records. In the few cases where dietetic notes were unavailable, clinician assessment of diet was accepted provided sufficient information was recorded prior to treatment. Abnormal diet was then classified as soft or more liquid diets. Patients who required therapeutic tube feeding prior to treatment were excluded.

Treatment details

Radiotherapy was planned with patients supine, immobilised by a 5 point thermoplastic mask. CT planning scans were undertaken in the treatment position, using IV contrast and 2–3 mm slices. This information was imported into Monaco® (Elekta) or Pinnacle (Philips) treatment planning systems, dependent on treatment centre. Differing protocols were in use at the time for target volume delineation and dose fractionation in each centre. All patients received bilateral neck treatment.

In Manchester, the standard dose for definitive radiotherapy was 66 Gray (Gy) in 30 fractions. A geometric approach was used for target volume delineation. Gross tumour volume (GTV) included the primary tumour and involved lymph nodes. High-dose clinical target volume (CTV) was defined as the GTV with an isotropic expansion of 10 mm, edited to natural anatomical boundaries without evidence of involvement. Intermediate-dose CTV included the remainder of the oropharynx, and involved nodal levels. Elective-dose CTV included the uninvolved but clinically at-risk nodal levels, as described below. A corresponding planning target volume (PTV) was created for each CTV by an isotropic expansion of 3 mm.

In Leeds, the standard dose for definitive radiotherapy was 70 Gy in 35 fractions. A compartmental approach to target volume delineation was adopted, in line with the approach in the PARSPORT study, and as previously described [21,22]. The primary tumour CTV included at least the GTV plus 10 mm and the anatomical compartment i.e. the whole oropharynx, edited to anatomical boundaries to exclude air and/or bone without evidence of invasion. The high-dose nodal CTV included the whole involved nodal level. Radiologically uninvolved nodal levels were treated at an intermediate or lower dose level according to clinician preference. A PTV was created by an isotropic expansion of 4 mm.

In both centres, the lymph node target routinely included levels Ib-V in the node-positive neck; nodal levels in a node-negative neck were selected depending upon tumour site and disease extent according to published recommendations [23]. Retropharyngeal lymph nodes were routinely included in cases with positive level II lymph nodes or pharyngeal wall involvement.

PTVs were required to receive 95–107% of the prescribed dose; 66 Gy in 30 fractions, or 70 Gy in 35 fractions for high dose volumes. Radiotherapy doses and organ at risk (OAR) constraints are detailed in Table 1. Intensity-modulated radiation therapy (IMRT) was used as standard to deliver treatment, using 6MV photons. Treatment verification was performed using a cone-beam CT scan for the first three treatments, and at least weekly thereafter.

Induction chemotherapy was given at clinician discretion, docetaxel, cisplatin and 5-fluorouracil (TPF) or, in four cases, cisplatin and 5-fluoruracil (PF). Standard concurrent chemotherapy was cisplatin (100 mg/m^2 given 3 weekly), and carboplatin (AUC5) was substituted if required, depending on renal function.

Patients treated in Leeds were managed with either a pre-treatment prophylactic gastrostomy or a reactive nasogastric feeding approach according to clinician and/or patient preference. In Manchester the approach of reactive nasogastric feeding as required was adopted. Patients were reviewed at least weekly by

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