Article:
Prestwich, RJD, Teo, MTW, Gilbert, A et al. (3 more authors) (2014) Long-term swallow function after chemoradiotherapy for oropharyngeal cancer: The influence of a prophylactic gastrostomy or reactive nasogastric tube. Clinical Oncology, 26 (2). 103 - 109. ISSN 0936-6555

https://doi.org/10.1016/j.clon.2013.10.005

*Title Page

Long term swallow function post-chemoradiotherapy for oropharyngeal cancer: the influence of a prophylactic gastrostomy or reactive nasogastric tube

Robin J D Prestwich[1], Mark T.W. Teo[1], Alexandra Gilbert[2], Gillian Williams[3], Karen E. Dyker[1], Mehmet Sen[1]

[1]Department of Clinical Oncology, St. James's Institute of Oncology, Leeds, UK

[2]University of Leeds, Leeds, UK

[3]Dietetic Department, St. James's Institute of Oncology, Leeds, UK

Corresponding Author:

Robin Prestwich

Email: Robin.Prestwich@leedsth.nhs.uk

Address: Level 4, St. James's Institute of Oncology, St. James's University Hospital, Beckett St., Leeds, LS9 7TF, UK

Tel: 0044 113 2067838

Fax: 0044 113 2067886

Long term swallow function post-chemoradiotherapy for oropharyngeal cancer: the influence of a prophylactic gastrostomy or reactive nasogastric tube

Abstract

Background

Two contrasting approaches of a prophylactic gastrostomy or a nasogastric tube as needed are widely used to support patients receiving chemo-radiotherapy for head and neck cancer. The influence of the type and timing of enteral feeding tube support upon long term swallowing is uncertain. This study analyses the patients' perspective on long term swallowing comparing two groups of patients who received chemoradiotherapy for oropharyngeal cancer managed with the two approaches.

Methods

The MD Anderson Dysphagia Inventory (MDADI) was posted to 63 consecutive patients with oropharyngeal squamous cell cancer treated with concurrent chemoradiotherapy between January 2007 and June 2009, who had not required therapeutic enteral feeding pre-treatment and who were disease free on follow up at least 2 years post-treatment.

Results

56/63 patients completed questionnaires; 43 had been managed with a prophylactic gastrostomy and 13 with a policy of NG tube as needed. There were no significant differences in all global, emotional, physical or functional domains of the MDADI according to enteral feeding strategy. Diet at 6 months post-treatment was significantly correlated with better MDADI scores.

Conclusions

In this study the choice of a prophylactic gastrostomy or NG tube as needed did not appear to influence long term swallowing function.

Introduction

Concurrent chemo-radiotherapy is the preferred treatment strategy for organ preservation for locally advanced head and neck squamous cell carcinoma (HNSCC). Trials have demonstrated a survival benefit for the addition of concurrent chemotherapy with the cost of increased treatment toxicity [1, 2]. Acute treatment related side effects of odynophagia, dysphagia, xerostomia and mucositis with associated weight loss are common. A large majority of patients require oral or enteral nutritional supplementation during and after treatment. The proportion of patients reported as requiring enteral feeding varies between reported series, with between 50-100% of patients receiving chemoradiotherapy needing enteral nutritional support [3-5]. Risk factors for requiring enteral feeding include pre-treatment weight loss and dysphagia, older age, large primary tumours, and treatment related factors including the use of concurrent chemotherapy and radiation dose to the pharyngeal constrictors [6, 7].

Two main approaches have been used to provide enteral nutrional support: i) prophylactic tube placement prior to treatment, and ii) reactive tube placement if and when required. A gastrostomy tube is usually preferred for the former approach and a nasogastric (NG) tube for the latter [6]. A recent UK based survey revealed no consensus as to which patients should be offered a prophylactic gastrostomy [8]. This remains a contentious area, and both approaches to enteral feeding have advantages and drawbacks. Several studies have suggested that the use of prophylactic gastrostomy placement is associated with a reduction in weight loss during treatment**,** a lower rate of hospitalisation [4, 9-11], and improved quality of life during and soon after treatment [12, 13]. Disadvantages of prophylactic gastrostomy placement prior to treatment include the possibility that the tube will not be required, a small risk of tube-related morbidity [14], and the uncertain influence upon long term enteral feeding dependency rates [6, 9-11, 15].

Long term swallowing outcomes are an important consideration in choosing the timing and method of providing nutritional support. Long term swallow function is an major factor influencing long term quality of life in survivors[6]. Mean radiation doses to the superior, middle and inferior constrictors along with the glottis and supraglottic larynx and oesophagus have been shown to correlate with long term swallow impairment [7]. The use of concurrent chemoradiotherapy is associated with clinically significant rates of severe long term dysphagia [16, 17]. For example, an analysis of 3 RTOG studies found 13% of patients were gastrostomy-dependent 2 years post treatment [16]. Several studies have reported a significantly increased duration of enteral feeding with prophylactic gastrostomies compared with a reactive enteral feeding approach [9, 10, 15, 18]. This has led to concern that the use of prophylactic gastrostomy tubes may lead to poorer long term swallow function [6, 11, 19]. However, there is very little data examining long term swallow function in relation to the route of enteral nutritional support during treatment.

We have previously reported the enteral feeding outcomes of a retrospective cohort of patients with oropharyngeal cancer patients treated with concurrent chemoradiotherapy [10]. Within this cohort were 71 patients managed with a prophylactic gastrostomy and 21 patients managed with an NG tube as needed; median duration of enteral feeding post-treatment was 181 versus 64 days respectively (p=0.01). We suggested that these data 'reinforce concerns regarding the detrimental impact of prophylactic gastrostomy placement upon long-term enteral feed dependence'. Duration of enteral feeding post-treatment is affected by many factors. It is unclear whether an increased duration of enteral feeding post-treatment is necessarily predictive of poorer long term swallow function. Here we report on the patients' perspective on long term swallow function in the same cohort, comparing these two strategies for enteral nutrition.

Methods

Study design

The study was registered with the Institutional Quality Improvement Board. In this single institution retrospective study, consecutive patients with locally advanced squamous cell carcinoma of the oropharynx treated with chemoradiotherapy between January 2007 and June 2009 were identified from electronic records. Inclusion criteria were: squamous cell carcinoma of oropharynx, treatment with curative intent (adjuvant or radical), and treatment with concurrent chemoradiotherapy, disease free on follow up for at least 2 years post-treatment. Patients were excluded if treatment was for recurrent disease, required therapeutic enteral feeding prior to treatment, disease recurrence at time of study. During this period of time, there was no policy at St. James's Institute of Oncology on the route and timing of enteral feeding; patients were managed with a prophylactic gastrostomy or a policy of a reactive NG tube based upon clinician and patient preference. Gastrostomies were either inserted endoscopically or radiologically guided, depending upon disease factors and local practice.

Patients included in the study were all more than 2 years following completion of treatment and were posted an explanatory letter along with the MD Anderson Dysphagia Inventory (MDADI) [20]. The MDADI is a validated self administered questionnaire designed for patients with head and neck cancer [20]. The MDADI consists of 20 questions and is divided into the following sub-scales: global, emotional, functional, and physical. The questions are shown in Table 1. The 1 to 5 point scoring for each question is described in the legend for Table 1. For each subscale (emotional, functional, physical) the scores are summed, and the mean score multiplied by 20 to provide a score with a range of 0-100 (with higher scores representing better functioning). The first question is scored individually in this manner to provide the global subscale. The MDADI questionnaire was sent a second time to non-responders after an interval of 2 months.

Data including oral intake (categorised as nil by mouth, sips, pureed diet, soft diet and normal diet), weight and the use of enteral feeding was routinely documented by the hospital dietetic team during treatment and during follow up by the local dietetic teams. Data (oral diet and enteral feeding) was collected by means of a proforma completed by the dietitians as previously described [10]. Data was requested at 6 weeks, 3, 6 and 12 months post radiotherapy in addition to the date of discontinuation of enteral feed.

Treatment details

Radiation therapy was delivered as previously described [21] using 6MV photons with a 3D conformal technique. Target volume routinely included bilateral level 1b-V lymph nodes and retropharyngeal lymph nodes at least at the level of the oropharynx. Intensity modulated radiotherapy was not utilised during the study period. The standard radical dose was 70Gy in 35 fractions; adjuvant treatment for high risk patients was with 66Gy in 33 fractions. Alternate dose fractionation schedules which were utilised are shown in Table 2. Induction chemotherapy was utilised at clinician discretion. Docetaxel, cisplatin and 5-flurouracil (TPF) and cisplatin and 5-fluorouracil (PF) were used as previously described [21, 22]. Standard concurrent chemotherapy was cisplatin 100 mg/m^2 days 1 and 29. Carboplatin AUC 4 was substituted for cisplatin if creatinine clearance was <55ml/min. During chemoradiotherapy all patients were reviewed twice weekly by medical and nursing teams, and if required by dietitian and speech and language teams.

Statistical analysis

Statistical analysis was performed using STATA software version 10 (Statacorp, Texas, USA). Duration of enteral feeding was defined from last day of radiotherapy treatment. A t test and chi square tests were used as appropriate to test for differences in subgroups analysed. MDADI scores were compared using a non-parametric Mann Whitney U test. A univariate

non-parametric analyses were performed to determine any correlation of MDADI scores with clinical variables. Variables were: age, T stage, N stage, overall stage, surgery, radiotherapy dose, diet pre-radiotherapy and at 6 weeks, 3 and 6 months post- radiotherapy. Statistical significance was declared at $p<0.05$.

Results

Patient, tumour and treatment details

104 patients were previously identified with oropharynx cancer treated with concurrent chemo-radiotherapy [8]. Of this cohort, 12 had required therapeutic enteral feeding prior to treatment and were excluded from this study. 63 of the remaining 92 patients were disease free with greater than two years post-treatment follow up. Completed MDADI were received from 56 out of 63 patients (89%). 43/56 (77%) had been managed with a prophylactic gastrostomy and 13/56 (23%) had been managed with a policy of NG tube as needed. All of these patients within the gastrostomy group received enteral feed. Three out of the 13 patients managed with a policy of NG tube as needed did not receive any enteral feed. Decisions regarding route of enteral feeding were made by the clinician and patient; during this period of time the clinical team generally favoured the use of prophylactic gastrostomies. Median follow up was 36.8 months (range 24.8 - 53.3 months). There was no significant difference in median follow up between the prophylactic gastrostomy group (36.4months, range 24.8-53.3 months) and the NG tube as needed group (35.9 months, range 24.8-52.9 months) (p=0.47). Table 2 summarises the patient demographics and tumour details for the prophylactic gastrostomy and NG as needed groups. The only statistically significant imbalance between the groups was a slightly higher body mass index (BMI) in the NG as needed group. There was no difference recorded in pre-treatment diet between the two groups. Treatment details are shown in Table 3.

Duration of enteral feeding

The median duration of enteral feeding post-radiotherapy was 161 days (95% CI 132-223) in the prophylactic gastrostomy group, and 53 days (95% CI 0-197) in the NG as needed group (p=0.68).

Analysis of MDADI scores

The global and domain specific MDADI scores in both groups of patients, who were all at least 2 years post-treatment, are shown in Table 4. Each domain is scored 0-100 with higher scores indicating better swallow function. The three subscales, emotional, physical and functional, evaluate swallowing limitations and the impact of swallow function upon quality of life. No significant differences were seen between MDADI scores in any domain between the prophylactic gastrostomy group and the NG tube as needed group.

On a univariate analysis, the variables age, T stage, N stage, overall stage, surgery, radiotherapy dose did not show any significant correlation with MDADI scores in any domain. Dietary information was available for 53/56 (95%) patients pre-radiotherapy, at end of radiotherapy and at 6 weeks post-radiotherapy, and for 47/56 (84%) patients 3 months post-radiotheray and 44/56 (79%) patients 6 months post radiotherapy. Only diet at 6 months post-radiotherapy showed a positive correlation with MDADI scores (for global score $p=0.05$, for physical score $p=0.05$, for emotional score $p=0.007$, for functional score $p=0.006$).

Discussion

Enteral feeding is commonly required to maintain weight during and for a period of time after chemoradiotherapy treatment for HNSCC. Prophylactic feeding tube placement compared with a reactive approach has been reported in several studies to reduce the extent of treatment related weight loss and hospital admissions [4, 9, 10], and to lead to improved short term quality of life [12, 13]. However, long term swallowing function is a major late toxicity associated with treatment, and should be a major factor in selecting the optimal strategy to support nutrition.

We and others have reported that prophylactic gastrostomies are associated with an increased duration of enteral feeding post-treatment [9, 10, 15, 18]. In a study of 120 chemoradiotherapy patients, Chen et al. found a 1 year gastrostomy use rate of 21% versus 0% in the prophylactic versus non-prophylactic gastrostomy group [18]. In our series of 104 oropharyngeal cancer patients treated with chemoradiotherapy, the enteral feeding rate 1 year post treatment was 20% versus 5% for the prophylactic gastrostomy versus NG tube as needed groups [10]. Protracted enteral feeding dependence may decondition the swallowing muscles, reducing the chances of returning to oral diet [17]. Concern about the detrimental impact of prophylactic gastrostomy tubes on long term swallow, despite their short term benefits, has led several centres to avoid prophylactic placement [6, 11]. Many factors influence the duration of enteral feeding, and it has not been demonstrated that the duration of enteral feeding post-treatment is a surrogate for long term swallow function.

This was a retrospective study examining swallowing specific quality of life outcomes in patients with oropharyngeal cancer who had not required therapeutic feeding pre-treatment, and who were disease free at least two years post-treatment. These results show that, as measured by the MDADI, there was no difference in long term swallowing function between patients managed with a prophylactic gastrostomy or an NG as needed. Patients were well-balanced in terms of baseline and treatment characteristics; pre-treatment diet was similar. The duration of enteral feeding was longer for the

group managed with a prophylactic gastrostomy, although likely due to the limited sample size, this difference was not statistically significant. Diet at 6 months post-treatment correlated with the MDADI scores. In view of the multiple comparisons, this correlation in a subgroup needs to be interpreted with caution. Interestingly this correlation was not seen with diet pre-radiotherapy, at the end of radiotherapy or 3 months post-treatment; these data suggest that the efforts to rehabilitate swallowing function are required for many months post treatment.

There are several limitations to our data. This was a retrospective analysis, and the selection of route of feeding was made on the basis of clinician and patient preference. Although baseline characteristics appear reasonably matched, it is not possible to exclude biases which may have influenced the choice of feeding route which may also influence long term swallowing function. The study group was heterogenous with regard to radiation doses and the number of cycles of concurrent chemotherapy administered; both of these factors are recognised to impact upon swallow function [7, 16]. For example, the slightly lower mean BMI in the prophylactic gastrostomy group may reflect a tendancy to choose this approach in patients who may be nutritionally compromised pre-treatment. The main outcome of the study is patients' self reported swallowing-related quality of life. There are several alternative tools which can be used to measure quality of life related swallowing outcomes, recently reviewed elsewhere [23]. The MDADI was selected for this study as a validated tool which examines patient reported outcomes as an important clinical endpoint. The inclusion of alternative measures would have been valuable but was limited by the retrospective nature of the study and concern that asking for excessive information would reduce the rate of questionnaire completion. The cohort of patients managed with an NG tube as needed is small, reflecting our practice of preferring prophylactic gastrostomies during this era. The radiotherapy technique employed in this era was 3D-conformal radiotherapy. Organ sparing intensity modulated radiotherapy has the potential to improve swallowing-related outcomes in the future [7].

There is little other data available to assess long term swallowing function in relation to enteral feeding strategies at the time of treatment. Corry et al. [9] found a non-significant increase in grade 3 dysphagia 6 months post-treatment (25% versus 8%). Similarly, Mekhail et al. [15] compared 62 gastrostomy-fed patients with 29 NG tube-fed patients, finding 30% versus 8% dysphagia rates 6 months post-treatment. However, dysphagia was measured in these studies at a relatively early timepoint for the assessment of a late toxicity. Oozeer et al. [24] also used the MDADI to assess swallowing function in patients with HNSCC more than 2 years following completion of chemoradiotherapy. Their study compared 16 patients managed with a prophylactic gastrostomy with 15 patients managed with an NG tube as needed; patients were matched for age, site and stage of tumour. The MDADI scores were significantly superior for the NG tube as needed group of patients. In their study mean scores for the prophylactic gastrostomy group versus the NG as needed group for each MDADI scale were: emotional 34 v. 61, functional 36 v. 84, physical 36 v. 61 and global 35 v. 60 ($p<0.001$for each scale) . Based on these results, the authors' concluded that in this matched cohort the 'use of gastrostomy tubes conferred a worse swallowing outcome in the long term'. Comparison with our results suggests that the MDADI scores for the prophylactic gastrostomy group (n=16) were markedly inferior than in our cohort (n=43). The reason for the differing outcomes of this and our study remain speculative. In interpreting these results it is important to consider that these relatively small studies took place in different centres with potential differences in factors such as patient selection for non-surgical treatment, treatment delivery and rehabilitation including dietetic and speech and language care.

Many factors are likely to influence long term swallowing function following chemoradiotherapy[6, 7, 25]. These include patient and tumour factors, smoking status, radiation technique, maintenance of oral intake during treatment, adherence to swallowing exercise regimens, and swallowing rehabilitation support provided. The timing and type of feeding tube is another factor which is likely to have an influence. These multiplicity of factors make comparison between differing series and institutions complex. Our data suggests that the

use of a prophylactic gastrostomy does not inherently lead to poorer long term swallowing function. We do acknowledge the limitation of retrospective data of this type and further prospective work is need in this controversial area. We consider it important that the use of any type of feeding tube is accompanied by an active programme to encourage early swallowing rehabilitation and discontinuation of enteral feeding; this support is required for a considerable period of time following completion of treatment.

References

1. Forastiere AA, Goepfert H, Maor M, Pajak TF, Weber R, Morrison W, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. N Engl J Med. 2003 Nov 27;349(22):2091-8.
2. Adelstein DJ, Li Y, Adams GL, Wagner H, Jr., Kish JA, Ensley JF, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J Clin Oncol. 2003 Jan 1;21(1):92-8.
3. Clavel S, Fortin B, Despres P, Donath D, Soulieres D, Khaouam N, et al. Enteral feeding during chemoradiotherapy for advanced head-and-neck cancer: a single-institution experience using a reactive approach. Int J Radiat Oncol Biol Phys. 2011 Mar 1;79(3):763-9.
4. Nguyen NP, North D, Smith HJ, Dutta S, Alfieri A, Karlsson U, et al. Safety and effectiveness of prophylactic gastrostomy tubes for head and neck cancer patients undergoing chemoradiation. Surg Oncol. 2006 Dec;15(4):199-203.
5. Wee Ho J. DM, Christian J. Outcomes of gastrostomy feeding tubes in patients undergoing primary chemoradiation for oral cavity, oropharynx, hypopharynx and larynx squamous cell carcinoma (SCC) at Nottingham University NHS Trust: a retrospective analysis 2004-2008. Clinical Oncology. 2011;23(3):S39.
6. Koyfman SA, Adelstein DJ. Enteral feeding tubes in patients undergoing definitive chemoradiation therapy for head-and-neck cancer: a critical review. Int J Radiat Oncol Biol Phys. 2012 Nov 1;84(3):581-9.
7. Eisbruch A, Kim HM, Feng FY, Lyden TH, Haxer MJ, Feng M, et al. Chemo-IMRT of oropharyngeal cancer aiming to reduce dysphagia: swallowing organs late complication probabilities and dosimetric correlates. Int J Radiat Oncol Biol Phys. 2011 Nov 1;81(3):e93-9.
8. Moor JW, Patterson J, Kelly C, Paleri V. Prophylactic gastrostomy before chemoradiation in advanced head and neck cancer: a multiprofessional web-based survey to identify current practice and to analyse decision making. Clin Oncol (R Coll Radiol). 2010 Apr;22(3):192-8.

9. Corry J, Poon W, McPhee N, Milner AD, Cruickshank D, Porceddu SV, et al. Prospective study of percutaneous endoscopic gastrostomy tubes versus nasogastric tubes for enteral feeding in patients with head and neck cancer undergoing (chemo)radiation. Head Neck. 2009 Jul;31(7):867-76.
10. Williams GF, Teo MT, Sen M, Dyker KE, Coyle C, Prestwich RJ. Enteral feeding outcomes after chemoradiotherapy for oropharynx cancer: a role for a prophylactic gastrostomy? Oral Oncol. 2012 May;48(5):434-40.
11. Paleri V, Patterson J. Use of gastrostomy in head and neck cancer: a systematic review to identify areas for future research. Clin Otolaryngol. 2010 Jun;35(3):177-89.
12. Salas S, Baumstarck-Barrau K, Alfonsi M, Digue L, Bagarry D, Feham N, et al. Impact of the prophylactic gastrostomy for unresectable squamous cell head and neck carcinomas treated with radio-chemotherapy on quality of life: Prospective randomized trial. Radiother Oncol. 2009 Dec;93(3):503-9.
13. Silander E, Nyman J, Bove M, Johansson L, Larsson S, Hammerlid E. Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer: a randomized study. Head Neck. 2012 Jan;34(1):1-9.
14. Grant DG, Bradley PT, Pothier DD, Bailey D, Caldera S, Baldwin DL, et al. Complications following gastrostomy tube insertion in patients with head and neck cancer: a prospective multi-institution study, systematic review and meta-analysis. Clin Otolaryngol. 2009 Apr;34(2):103-12.
15. Mekhail TM, Adelstein DJ, Rybicki LA, Larto MA, Saxton JP, Lavertu P. Enteral nutrition during the treatment of head and neck carcinoma: is a percutaneous endoscopic gastrostomy tube preferable to a nasogastric tube? Cancer. 2001 May 1;91(9):1785-90.
16. Machtay M, Moughan J, Trotti A, Garden AS, Weber RS, Cooper JS, et al. Factors associated with severe late toxicity after concurrent chemoradiation for locally advanced head and neck cancer: an RTOG analysis. J Clin Oncol. 2008 Jul 20;26(21):3582-9.
17. Lee WT, Akst LM, Adelstein DJ, Saxton JP, Wood BG, Strome M, et al. Risk factors for hypopharyngeal/upper esophageal stricture formation after concurrent chemoradiation. Head Neck. 2006 Sep;28(9):808-12.

18. Chen AM, Li BQ, Lau DH, Farwell DG, Luu Q, Stuart K, et al. Evaluating the role of prophylactic gastrostomy tube placement prior to definitive chemoradiotherapy for head and neck cancer. Int J Radiat Oncol Biol Phys. 2010 Nov 15;78(4):1026-32.
19. Corry J. Feeding tubes and dysphagia: cause or effect in head and neck cancer patients. J Med Imaging Radiat Oncol. 2009 Oct;53(5):431-2.
20. Chen AY, Frankowski R, Bishop-Leone J, Hebert T, Leyk S, Lewin J, et al. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the M. D. Anderson dysphagia inventory. Arch Otolaryngol Head Neck Surg. 2001 Jul;127(7):870-6.
21. Prestwich RJ, Oksuz DC, Dyker K, Coyle C, Sen M. Feasibility and Efficacy of Induction Docetaxel, Cisplatin, and 5-Fluorouracil Chemotherapy Combined with Cisplatin Concurrent Chemoradiotherapy for Nonmetastatic Stage IV Head-and-Neck Squamous Cell Carcinomas. Int J Radiat Oncol Biol Phys. 2011 May 26.
22. Prestwich RJ, Kancherla K, Oksuz DC, Williamson D, Dyker KE, Coyle C, et al. A single centre experience with sequential and concomitant chemoradiotherapy in locally advanced stage IV tonsillar cancer. Radiat Oncol. 2010;5:121.
23. Kanatas AN, Rogers SN. A guide of the questionnaires used in the measurement of health-related quality of life in head and neck oncology. Tumori. 2008 Sep-Oct;94(5):724-31.
24. Oozeer NB, Corsar K, Glore RJ, Penney S, Patterson J, Paleri V. The impact of enteral feeding route on patient-reported long term swallowing outcome after chemoradiation for head and neck cancer. Oral Oncol. 2011 Oct;47(10):980-3.
25. Bhayani MK, Hutcheson KA, Barringer DA, Lisec A, Alvarez CP, Roberts DB, et al. Gastrostomy tube placement in patients with oropharyngeal carcinoma treated with radiotherapy or chemoradiotherapy: Factors affecting placement and dependence. Head Neck. 2013 Jan 16.

Table

Table 1: The M.D. Anderson Dyphagia Inventory (MDADI). There are five possible answers to each question: strongly agree, agree, no opinion, disagree, strongly disagree. Answers are scored on a scale 1 to 5. Questions E7 and F2 are scored 5 points for strongly agree and 1 point for strongly disagree. All other questions are scored as 1 point for strongly agree and 5 points for strongly disagree. Questions are divided into subscales (global, emotional (E), functional (F) and physical (P)).

Subscale	Question
Global	My swallowing ability limits my day-to-day activities.
E2	I am embarrassed by my eating habits.
F1	People have difficulty cooking for me.
P2	Swallowing is more difficult at the end of the day.
E7	I do not feel self-conscious when I eat.
E4	I am upset by my swallowing problem.
P6	Swallowing takes great effort.
E5	I do not go out because of my swallowing problem.
F5	My swallowing difficulty has caused me to lose income.
P7	It takes me longer to eat because of my swallowing problem.
P3	People ask me, ‘Why can’t you eat that?’
E3	Other people are irritated by my eating problem.
P8	I cough when I try to drink liquids.
F3	My swallowing problems limit my social and personal life.
F2	I feel free to go out to eat with my friends, neighbours, and relatives.
P5	I limit my food intake because of my swallowing difficulty.
P1	I cannot maintain my weight because of my swallowing problem.
E6	I have low self-esteem because of my swallowing problem.
P4	I feel that I am swallowing a huge amount of food.
F4	I feel excluded because of my eating habits.

Table 2: Patient and tumour characteristics

	Prophylactic gastrostomy (N=43)	NG as needed (N=13)	P-value
Age (Median, range)	54 (41 – 71)	58 (43 – 68)	0.34
Sex			
Male	33 (77%)	7 (54%)	
Female	10 (23%)	6 (46%)	
WHO PS			
0	36 (83.7%)	8 (61.5%)	0.07
1	5 (11.6%)	5 (38.5%)	
Not recorded	2 (4.7%)	0 (0%)	
Smoking			
Never	14 (32.6%)	2 (15.4%)	0.53
Ex	12 (27.9%)	5 (38.5%)	
Current	14 (32.6%)	4 (30.8%)	
Not recorded	3 (7.0%)	2 (15.4%)	
Weight: Mean/kg (range)	84.4 (57.4 - 109.4)	77.8 (65.2 - 120.5)	0.91
Body mass index: Mean (range)	27.9 (19.2 - 34.8)	29.7 (22.6 - 38.5)	0.02
Oropharynx subsite			
Tonsil	29 (67.4%)	8 (61.5%)	0.19
BOT	14 (32.6%)	4 (30.8%)	
Uvula	0 (0%)	1 (7.7%)	
T stage			
T1	12 (27.9%)	4 (30.8%)	0.56
T2	11 (25.6%)	4 (30.8%)	
T3	6 (14.0%)	0 (0%)	
T4	14 (32.6%)	5 (38.5%)	
Nodal stage			
N0	3 (7.0%)	0 (0%)	0.69
N1	6 (14.0%)	1 (7.7%)	
N2	32 (74.4%)	11 (84.6%)	
N3	2 (4.6%)	1 (7.7%)	
Stage			
III	5 (11.6%)	0 (0%)	0.20
IV	38 (88.4%)	13 (100%)	
Histology			
SCC	43	13	NA
Pre-treatment oral intake			
NBM	0 (0%)	0 (0%)	0.18
Sips	0 (0%)	0 (0%)	
Pureed	0 (0%)	1 (7.7%)	
Soft	6 (14.0%)	2 (15.4%)	
Normal	37 (86.0%)	10 (76.9%)	

Table 3: Treatment characteristics

	Prophylactic gastrostomy (N=43)	NG as needed (N=13)	P-value
Surgery			
No	42 (97.7%)	12 (92.3%)	0.36
Yes	1 (2.3%)	1 (7.7%)	
Induction chemotherapy			
TPF	17 (39.5%)	2 (15.4%)	0.26
PF	6 (14%)	2 (15.4%)	
None	20 (46.5%)	9 (69.2%)	
Radiotherapy dose prescription			
70Gy in 35 fractions	39 (90.7%)	10 (76.9%)	0.40
66Gy in 33 fractions	1 (2.3%)	0 (0%)	
65Gy in 30 fractions	2 (4.7%)	2 (15.4%)	
55Gy in 20 fractions	1 (2.3%)	1 (7.7%)	
Concurrent chemotherapy			
Cisplatin	43 (100%)	10 (76.9%)	0.004
Carboplatin	0 (0%)	3 (23.1%)	
No. of cycles			
1	8 (18.6%)	5 (38.5%)	0.32
2	32 (74.4%)	7 (53.8%)	
3	3 (7%)	1 (7.7%)	

Table 4: MDADI scores according to intended enteral feeding route

	Whole cohort (N=56)	Prophylactic gastrostomy (N=43)	NG as needed (N=13)	P-value
Global:				
Median (Range)	40 (0 - 100)	40 (0 - 100)	40 (20 - 100)	0.58
Physical:				
Median (Range)	55 (17.5 - 100)	55 (17.5 - 100)	52.5 (25 - 100)	0.49
Emotional:				
Median (Range)	66.7 (20 - 100)	68.3 (20 - 100)	50 (20 - 100)	0.42
Functional:				
Median (Range)	64 (20 - 100)	70 (20 - 100)	48 (32 - 100)	0.21

*Author agreement form

CLINICAL ONCOLOGY

AUTHORSHIP RESPONSIBILITY, FINANCIAL DISCLOSURE & CONTRIBUTORSHIP

Manuscript No: 13-0524R1

Corresponding author's name: ROBIN PRESTWICH
Address: Level 4 Bexley Wing, St. James's Institute Oncology
Beckett St, Leeds LS9 7TF
Tel: 0113 2067838 Fax: 0113 2067886 E-mail: Robin.Prestwich@leedsth.nhs.uk

By signing this form, each author affirms that he/she has read and agrees to all authorship responsibility, contributorship, and financial disclosure/conflict of interest matters.

1. Authorship responsibility (***to be signed by all named authors at the bottom of this form***): My signature certifies that I have participated sufficiently in the conception and design of this work, the analysis of the data (where applicable) as well as the writing of the manuscript to take public responsibility. The manuscript represents valid original work. I attest that that the work described has not been published before (except in the form of an abstract or as part of a published lecture, review or thesis). It is not under consideration elsewhere, nor will it be submitted for publication elsewhere while under consideration by *Clinical Oncology*. I have reviewed this manuscript and approve its submission. The undersigned authors also warrant that this work contains no libellous or unlawful statements, does not infringe on the rights of others, or contains material or instructions that might cause harm or injury.

2. Financial Disclosure/Conflict of Interest: By signing below I certify that any affiliations with or involvement in any organisation with a direct financial interest in the subject matter or materials discussed in the paper are noted below. Otherwise my signature indicates that I have no such financial interest. All funding or project support is acknowledged in the manuscript.

Statement of Financial Interest: (please use additional sheet if necessary)

_____
_____
_____
_____

4. Contributorship: Please list each authors' contribution to the above manuscript. Please provide details such as, the original idea for the research, which individual(s) undertook the collection of data, proportion of patients entered by an individual, responsibility for the first draft of the manuscript, etc.

Author 1 Original idea, data collection, 1st draft manuscript, revision

Author 2 Data analysis, manuscript preparation

Author 3 Data collection, analysis, manuscript review

Author 4 Data collection, analysis, manuscript review

Author 5 Concept, Manuscript review

Author 6 Concept, Manuscript review

Please also give details of persons (who may not be on the list of authors) who provided statistical advice for the data from the inception of the study and undertook statistical analyses.

Signatures

Author 1 _____ Date 2/8/13

Author 2 _____ Date 2/8/13

Author 3 _____ Date 5.8.13

Author 4 _____ Date 7.8.13.

Author 5 _____ Date 2.8.13

Author 6 _____ Date 7/8/13