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Predictors of swallowing outcome in patients treated with surgery and radiotherapy for advanced oral and oropharyngeal cancer

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SUMMARY

Retaining effective swallowing is a key element when optimising outcomes in the management of head and neck cancer. We report the functional swallowing outcomes for a cohort of 31 individuals with advanced oral and oropharyngeal cancer who underwent free or pedicled flap reconstruction of surgical defects. Swallowing was assessed pre and immediately post surgery and at four months post treatment. Swallowing assessments were related to site, size and volume of defect and composition of flap reconstruction. The effect of radiotherapy on swallowing was assessed among 17 of the 31 individuals who were submitted to radiotherapy after surgery.

The proportion of patients on a total oral diet four months post treatment varied significantly by site of defect (Fishers exact test $p = 0.006$), from 100% (7/7) of patients with a lateral defect to only 22% (2/9) of patients with a central defect.

The proportion of patients on a total oral diet at the final assessment did not vary by flap reconstruction or radiotherapy.

Introduction

Oral & oro-pharyngeal cancer and its subsequent treatment have a significant deleterious effect on an individual's swallowing. Tumour characteristics such as T stage and site have been implicated in swallowing impairment [1–3]. In addition features specific to the cancer treatment, whether that treatment is surgery, radiotherapy, chemo radiation or a combination, have been demonstrated to impact on an individual's swallowing [4–10].

Surgical management of oral and oro-pharyngeal tumours frequently necessitates reconstruction of lost tissues for oral continuity and functional reasons [11]. This reconstruction commonly involves free tissue transfer, and to a lesser extent regional pedicled tissue transfer [11–14]. The extent and nature of dysphagia may depend on the tumour site and the type of reconstruction [11,12,15,16].

Adjuvant radiotherapy or chemo/radiotherapy may be necessary in a significant proportion of oral and oro-pharyngeal tumours, particularly larger T stage lesions and this may produce a compounding adverse effect on swallowing [17]. Radiotherapy induces damage in normal tissues of the oral cavity and oropharynx resulting in reduced salivary flow and fibrosis in the irradiated field [18].

Swallowing outcomes in patients undergoing resection and reconstruction have been examined in both pre-treatment and post treatment groups, however little has been published relating to swallowing assessments spanning the treatment period [6,16,19,20]. Markkanen-Leppanen et al. (2005) did undertake such an assessment; however their analysis focused on the impact of free flap reconstruction sensation [21] rather than the potential contributors to swallowing dysfunction.

The aim of this retrospective review was to assess the impact of certain tumour characteristics and treatment parameters on swallowing function as defined by oral intake in oral and oro-pharyngeal cancer patients. The amount and type of oral intake was determined at the time of presentation and subsequently monitored across the period of treatment following primary surgery with or without radiotherapy. The changes in swallow function related to both the site and the volume of the primary tumour and to the reconstructive method utilised were investigated.

In addition, the effect of postoperative radiotherapy (where employed) on swallowing was evaluated.

Patients and methods

Patients

A retrospective review of the clinical notes and swallowing assessment data was made for a cohort of individuals diagnosed with advanced oral or oropharyngeal cancer between August

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2005 and February 2007 at the Head & Neck Centre of University College Hospital London. Inclusion criteria for enrolment in the study were stage III–IV oral or oropharyngeal malignancy which underwent surgery and subsequent reconstruction with either free or regional tissue transfer with or with out postoperative radiotherapy. All individuals were required to have completed a minimum 4 month postoperative period and had swallowing assessments at three specific time points spanning their treatment period.

Fifty-nine consecutive patients were treated surgically for advanced oral or oropharyngeal cancer between August 2005 and February 2007. Thirty-one had swallowing assessments at the three time points and were included in this study.

Site of disease, classification and reconstruction modality

The oral cavity and oropharynx were divided into four anatomical-functional areas: Lateral (lateral floor of mouth, mandibular body or buccal cavity), Anterior (anterior floor of mouth, inter canine segment of mandible, labial vestibule), Central (hemi-, or total tongue) and Oropharyngeal (retromolar trigone, soft palate and tonsillar fossa area). Each resection was characterised to one of the four areas for comparison (Fig. 1).

Reconstruction varied according to site, size, volume, and composition of the defect and with respect to intrinsic patient features such as suitability for free tissue transfer. The reconstruction employed was categorised to one of three categories depending on their composition: fascio-cutaneous (radial forearm and anterolateral thigh flap), myocutaneous (latissimus dorsi and pectoralis major flap) or composite – bone and soft tissue containing flaps (fibula and scapula osseo-cutaneous flap or DCIA bone with internal oblique muscle flap).

Swallow evaluation

Swallow assessment data for each individual was retrieved from the clinical case notes and merged with information from the departmental database of head & neck cancer patients. This

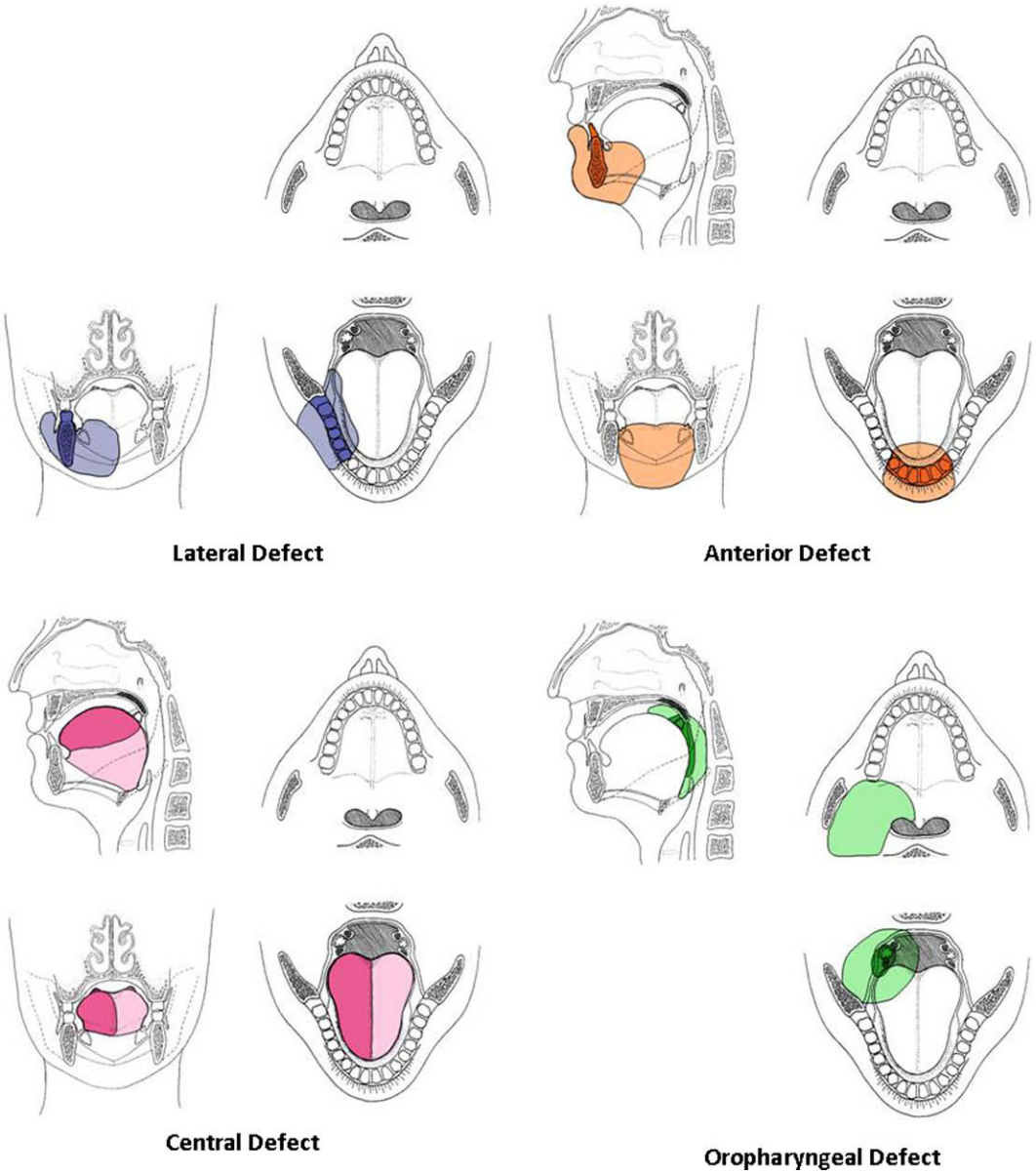

Figure 1 Schematic representation of four classifications for site of disease (modified from Nicoletti [16]).

Table 1
Functional oral intake score categories.

FOIS Grade	Intake description
Grade 1	Nothing by mouth
Grade 2	Tube dependent with minimal attempts of food or liquid
Grade 3	Tube dependent with consistent oral intake of food or liquid
Grade 4	Total oral diet for a single consistency
Grade 5	Total oral diet with multiple consistencies, but requiring special preparation, but with specific food limitations
Grade 6	Total oral diet with multiple consistencies without special preparation, but with specific food limitations
Grade 7	Total oral diet with no restrictions

database holds details of patient demographics, tumour specifics (including site, size & volume), and treatment modalities and reconstructive methods where surgery was undertaken (regional vs. free tissue transfer, single tissue vs. composite defect reconstruction).

Each patient was scored, pre and immediately post surgery and at four months after surgery and/or completion of radiotherapy using the Functional Oral Intake Score (FOIS) [22] (Table 1).

The allocation to a specific FOIS point was based on oral intake recommendations from either videofluoroscopy swallow or bedside examinations. This scoring of individuals oral intake was undertaken at each of three points spanning the individual's treatment and follow up (preoperative, immediate postoperative and four months postoperative or following completion of radiotherapy). Patients were also assessed to be tube dependent (FOIS grades 1–3) or on an oral diet (FOIS grades 4–7).

Statistical analysis

The analysis of the data of the 31 individuals included in the study was mainly a descriptive single variable analysis. The data was summarised using simple descriptive statistics: frequency distributions for categorical data and mean, standard deviation (s.d.), median, and interquartile range for continuous data.

Categorical variables were tabulated against the preoperative, postoperative and final FOIS scores and analysed using the chi-squared test or Fisher's exact test. Continuous variables were analysed using one way analysis of variance, the unpaired *t*-test or Wilcoxon rank-sum test as appropriate. Single and multivariable logistic regression was used to analyse the binary variable, final swallowing (that is whether the patient was tube dependent or on an oral diet at the four month assessment). Site of defect, size of defect, volume of defect, and flap reconstruction were the explanatory variables with age at operation, sex, and radiotherapy included as co-variants.

All variables were assessed at the 5% significance level with no correction for multiple testing. Any statistically significant results should be treated with caution and re-assessed in a larger dataset.

Results

Patient characteristics

Of the 31 individuals who had their swallowing assessed 20 were men (64.5%). The mean age at time of presentation was 55.4 years (s.d. 12.1, range, 24.6–76.6). There was no significant difference in age between men and women.

The site of defect was lateral (7), oropharyngeal (11), central (9), and anterior (4). Overall the defect size ranged from 8.8 cm^2 to 67.6 cm^2 and the defect volume ranged from 9 cm^3 to 244.2 cm^3. Defect size and volume are summarised in Table 1. Neither varied significantly by site of defect although two of the four anterior tumours were the second and third largest overall.

Table 2
Characteristics of the tumour and resection.

Characteristic Tumor Site	Number of patients (%)	Size of defect (cm^2) Mean (s.d.)	Volume of defect (cm^3) Mean (s.d.)
Lateral	7 (23)	37.7 (20.0)	130.5 (77.2)
Anterior	4 (13)	50.7 (22.3)	140.1 (72.7)
Central	9 (29)	34.9 (16.0)	116.5 (76.0)
Oropharyngeal	11 (35)	36.7 (16.6)	107.0 (62.5)
Total	31 (100)		
Flap Reconstruction			
Fasciocutaneous	15 (48)	26.1 (12.3)	68.9 (49.3)
Musculocutaneous	10 (32)	51.8 (13.0)	170.4 (46.9)
Composite	6 (19)	45.9 (16.7)	160.2 (51.4)
Total	31 (100)		

The type of reconstruction undertaken was facio-cutaneous in fifteen individuals, musculo-cutaneous in ten cases, and composite (soft tissue and bone) in the remaining six. Defect size and volume varied significantly by type of flap reconstruction, both $p < 0.001$. There was no difference in volume or size of defect between musculo-cutaneous and composite reconstruction, but the defects were significantly smaller, in both volume and size, for facio-cutaneous reconstructions (Bonferroni adjusted *t*-tests comparing facio-cutaneous to musculo-cutaneous and composite reconstruction all $p < 0.02$), see Table 2.

17 (54.8%) of the 31 individuals received postoperative radiotherapy. The proportion of patients receiving postoperative radiotherapy varied significantly by the site of the defect (Fisher's exact test $p = 0.005$). All patients with a central defect received radiotherapy (9/9), compared to 45.4% (5/11) of those with an oropharyngeal defect, 28.6% (2/7) of those with a lateral defect and 25% (1/4) of those with an anterior defect.

The site of defect, flap reconstruction undertaken, and radiotherapy did not vary by sex, and there were no significant differences in mean size of defect, or mean defect volume by sex.

Swallowing assessment

Swallowing function was assessed at three time points; pre-surgery, post-surgery, and four months postoperatively. The FOIS grade at each time by site of defect is given in Fig. 2.

It is apparent that patients with central or anterior defects had much worse swallowing outcomes at four months than patients with oropharyngeal or lateral defects: the mean FOIS grades at four months were; central, 2.4 and anterior, 2.8, compared to oropharyngeal, 4.8 and lateral, 6.4. The mean FOIS scores for patients with central and anterior defects dropped more between pre-operation and four months after operation than for patients with oropharyngeal and lateral defects. Mean four month FOIS grades were 1.9 points (central) and 2.2 points (anterior) lower than the mean pre-operation grades, whereas the mean four month FOIS grades were only 0.8 points (oropharyngeal) and 0.6 points (lateral) lower.

At all sites the mean FOIS grade dropped post surgery, and at no site did all patients regain their pre-operation grade.

There was no significant difference in volume or size of defect by defect site or tube dependency at any of the three time points.

Of the 17 (55%) patients who underwent postoperative radiotherapy none showed a deterioration of their FOIS score between the immediate postoperative swallow assessment and the final swallow assessment, whilst 8 improved. By comparison the non-radiotherapy group had 1 individual with deterioration in FOIS score and two with improvements.

The difference in change in swallowing between patients receiving radiotherapy and those not, did not reach statistical significance ($p = 0.07\%$).

Analysis of tube dependency four months post surgery (final swallowing assessment - tube dependent or total oral diet).

14 (45%) of the 31 patients were still tube dependent at the four month postoperative assessment. The distribution of tube dependency according to reconstructive technique is given in Table 3. There was no significant difference in the proportion of patients who were tube dependent at four months by reconstructive technique (Fisher's exact test, $p = 0.635$).

There was a significantly higher proportion of females tube dependent four months post-surgery than males, 72.7% (8/11) of the females and 30% (6/20) of the males, Fishers exact test $p = 0.03$. The age of tube dependent patients at four months was not significantly different from those on a total oral diet, mean 58.5 (s.d. 10.7) and 52.8 (s.d. 12.9) respectively, unpaired t-test $p = 0.1979$.

There was no difference in the size and volume of the defects by final FOIS scores, one way analysis of variance $p = 0.4624$ and $p = 0.1959$, respectively. The mean (s.d.) for size for tube dependent and total oral diet were 40.8 (17.9) cm^2 and 36.0 (17.8) cm^2, respectively. The mean (s.d.) for volume for tube dependent and total oral diet were 137.1 (64.6) cm^3 and 104.7 (70.2) cm^3, respectively.

The proportion of patients on a total oral diet at four months varied significantly by site of defect (Fisher's exact test $p = 0.006$). All seven patients with a lateral defect, 63.6% (7/11) with an oropharyngeal defect, 22.2% (2/9) with a central defect, and 25% (1/4) with an anterior defect were on a total oral diet. The proportion of patients on a total oral diet at the final assessment did not vary by radiotherapy.

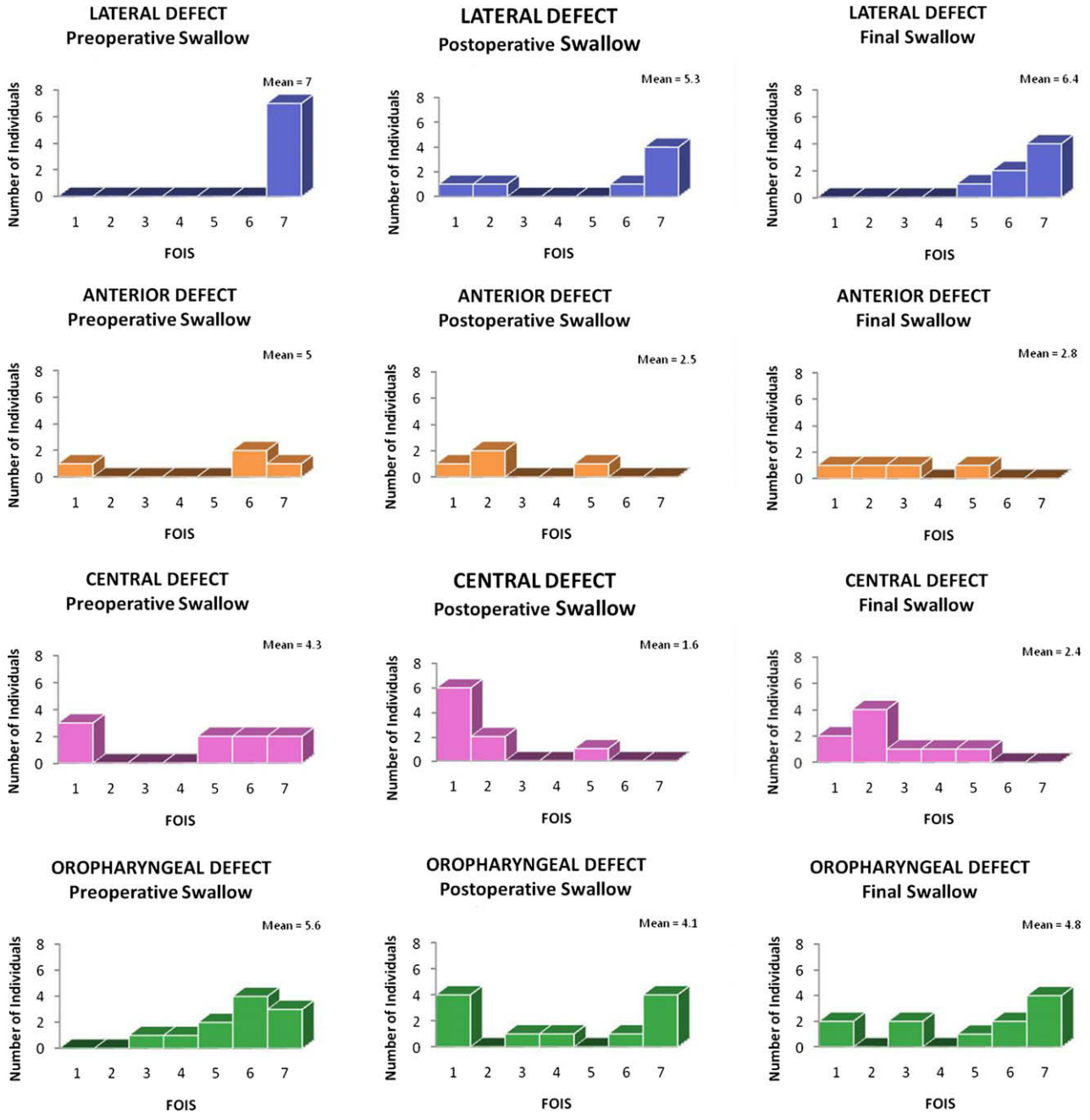

Figure 2 FOIS score by defect site across the treatment period (preoperative, immediate postoperative and final swallow at four months post treatment).

Table 3
Grouped outcome swallow by flap composition.

		Flap composition		
Group oral intake status	Fascio-cutaneous	Musculo-cutaneous	Composite	TOTAL
Tube dependent FOIS (1–3)	6 (40.0%)	6 (60.0%)	2 (33.3%)	14 (45.2%)
Oral diet FOIS (4–7)	9 (60.0%)	4 (40.0%)	4 (66.7%)	17 (54.8%)
TOTAL	15 (100%)	10 (100%)	6 (100%)	31 (100%)
Fisher's exact=				

Confirmatory single variable logistic regression analysis showed that the only variable significantly related to the final swallowing assessment (i.e. the proportion tube dependent), apart from sex which is regarded as a covariate, was site of defect. Investigatory multivariable logistic regressions on each explanatory variable separately, first with age and sex as covariates and secondly with radiotherapy as a covariate, confirmed site of defect to be the only variable significantly related to the final swallowing assessment.

Discussion

Swallowing function in a cohort of individuals undergoing surgical ablation and reconstruction for oral and oropharyngeal malignancy was investigated both before and after treatment and the contributors to swallowing outcome assessed.

As had been highlighted previously in the literature, site of surgical defect has a significant impact on swallowing. Nicoletti et al. [16] reported a functional evaluation of 196 individuals after surgery for oral malignancy and found site to contribute a strong negative impact on outcome and also to the extent of recovery of deficit over time. Both site and size of defect were shown by Pauloski et al. [6] to have a negative bearing on swallowing in a group of 144 patients where swallowing was assessed three months post surgery. When assessing the postoperative swallowing of a cohort of 80 patients Borggreven et al. [19] found that profound swallowing complications were again site related. In particular combined resections of the tongue and soft palate had particularly poor swallowing outcomes. Free flap reconstruction had been undertaken in all cases. Our results reflect the findings of these and others [9,15,23], with site being shown to be a significant prognostic indicator for long term swallowing function.

The size and volume of defects reconstructed showed no significant effect on outcome swallow in this retrospective study. Similarly the type of flap utilised to reconstruct defects showed no significant difference in terms of final swallowing outcome. Kariwala et al. [24] found only minimal effects of defect size and type of flap in their study of 191 head and neck reconstructions cases. The relatively small number of individuals in this study may have an implication in our findings. However, we would argue that the selection of flap type when reconstructing should be tissue specific rather than site or composition dependent.

The provision of radiotherapy to patients varied by site ($p = 0.005\%$). However, in contrast to previous evidence [2,10,18,25], the swallowing outcomes were not worse in the radiotherapy group, the proportion of patients whose swallowing improved over the four month postoperative period was 14% (2/14) among patients not receiving radiotherapy compared to 47% (8/17) among those who did,. Nevertheless, this may reflect the impact of time on the swallowing assessment as the patients undergoing radiotherapy had the swallowing assessed after the completion of radiotherapy however this did not reach statistical significance at the 5% level. In addition, this may be a reflection of the small study numbers and the number of variables requiring analysis.

This study attempted to determine the effect of oral and oropharyngeal tumours across the full period of management; from the preoperative phase through to the recovery and rehabilitation phase.

There were no statistically significant results reflecting recovery of swallowing being better in one site over another. We believe, however that this should be tested in a larger cohort of individuals in a prospective manner and it is an area yet to be reported on in the literature.

Conclusion

In our experience, the site of a tumour and the defect resulting from surgical management of oral tumours are significant determinants of postoperative swallowing, although only the former was detected here.

This relatively small retrospective analysis of functional swallowing data lends weight to an argument for a larger prospective study aimed at further investigating the interaction between site of tumour and reconstruction across the entire treatment period; preoperative through to rehabilitation.

Although trends were highlighted, a larger study is needed to determine the significance of the tumour itself and the effects of ablative treatment.

This study contributes to the guidance for those involved with management of advance oral and oropharyngeal tumours and the subsequent surgical defects. In addition it offers further information to provide improved understanding in preoperative patients with respect to the expected outcomes following treatment.

Conflict of interest statement

None declared.

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