# Pre-treatment Risk Stratification of Feeding Tube Use in Patients Treated with IMRT for Head and Neck Cancer

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**Conflict of interest**

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**Abstract**

Purpose: To establish a risk stratification model for feeding tube (FT) use in head and neck IMRT patients.

Methods: 139 patients treated with definitive IMRT (+/- concurrent chemotherapy) for head and neck mucosal cancers were included. Patients were recommended a prophylactic FT and followed up by a dietician for at least eight weeks post-radiotherapy. Potential prognostic factors were analysed for risk and duration of FT use for at least 25% of dietary requirements.

Results: Many variables had significant effects on risk and/or duration of FT use in univariate analyses. Subsequent multivariable analysis showed that T-classification ≥ 3 and level 2-lymphadenopathy were the best independent significant predictors of higher risk and duration of FT use respectively in oral cavity, pharynx and supraglottic primaries.

Conclusions: In patients treated with definitive IMRT, T-classification ≥ 3 and level 2-lymphadenopathy can potentially stratify patients into four risk groups for developing severe dysphagia requiring FT use.

**Introduction**

Head and neck cancer and its treatment with radiation therapy (RT), with or without concurrent chemotherapy, are associated with dysphagia and associated malnutrition and weight loss.[1-4] Enteral feeding via a feeding tube (FT) is a common method of providing patient nutrition during and immediately following RT in as many as 80% of patients. [5-9] Patients at high risk of prolonged, severe dysphagia may benefit from a prophylactic gastrostomy tube to minimize hospitalisations, while maximising convenience and short term quality of life.[10-12] .

However, the insertion of a gastrostomy tube is an invasive procedure which can be associated with major complications and occasionally death.[13] Prolonged use of gastrostomy tubes has been associated with long-term swallow dysfunction and a potential risk of late mortality. [11,14]Considering these risks, the insertion of prophylactic gastrostomy tubes should be reserved for those patients likely to derive the most benefit, namely patients at highest risk of prolonged, severe dysphagia. Furthermore, identification of high risk patients is critical in developing patient pathways and appropriate allocation of allied health resources. The main objective of this study was to develop a risk stratification model for anticipated duration of FT use, using the clinical and radiological information available at a patient's initial discussion at a Multidisciplinary Tumor Board.

**Methods and Materials**

*Patients*

Following Institutional Ethics Committee approval, the patient population was retrospectively accrued from the institution's radiation oncology database. To be eligible for inclusion, patients were required to receive primary and definitive intensity-modulated radiotherapy (IMRT) (with or without concurrent systemic treatment) for mucosal cancers of the head and neck. Patients with stage II–IVB disease were included. Patients were excluded if they underwent therapeutic surgery to the primary site or neck dissection prior to commencing RT. Patients were required to have been offered a prophylactic FT prior to treatment, as per departmental policy- laryngeal and pharyngeal tumors planned to receive ≥64Gy with bilateral nodal

irradiation, or having a pre-existing nutritional deficiency. All included patients had to be followed up by a dietician for a minimum of eight weeks post radiotherapy completion.

*Pre-treatment evaluation*

Prior to treatment, each patient underwent diagnostic contrast-enhanced computed tomography (CECT) of the face, neck and chest, as well as whole-body positron emission tomography with low dose CT for co-registration (PET/CT). Selected patients underwent magnetic resonance imaging (MRI) through the face and neck, when it was thought clinically beneficial to assist in optimal target delineation, e.g. nasopharyngeal primary disease.

*RT planning and treatment*

Target volumes were outlined on the planning CECT by one radiation oncologist. The PET/CT and MRI (if available) were co-registered with the planning CECT on the treatment planning system (TPS). The elective (prophylactic) nodes were defined according to consensus guidelines.[15] All patients received bilateral, elective irradiation of levels 2 to 4 nodes. Patients with oropharynx or nasopharynx cancers had bilateral, elective irradiation of level 1B nodes. In patients with oropharynx or hypopharynx cancers elective irradiation of ipsilateral level 5 nodes and the retrostyloid space was delivered to clinically node positive hemi-necks. In patients with cancer of the nasopharynx, bilateral retrostyloid space lymph nodes were treated to an elective dose. All T0 patients in this cohort were treated electively to bilateral nodal basins, including level 1B, while bilateral tonsils and tongue base were treated as high risk clinical target volume (CTV).

Clinically and radiologically involved nodes were contoured individually. The prescribed doses were planned with a simultaneous integrated boost to a gross tumor volume (GTV), high riskCTV and low risk CTV. In 137 cases, the dose to GTV (66–70Gy), high risk CTV (63Gy) and elective CTV (56Gy) was planned at five fractions per week over six to seven weeks. The remaining two patients were prescribed 60 or 64Gy in 30 fractions. Medically fit patients were considered for concurrent systemic therapy based on disease stage and comorbidities.

Optimized IMRT plans, deliverable via seven to nine equally spaced step-and-shoot segmented beams on a 6 MV linear accelerator (Elekta Synergy, Elekta, Crawley, UK), were generated using either the Elekta CMS XiO or Monaco treatment planning systems (TPS) (Elekta, St Louis, MO, USA) on 0.25 cm CT slices.

*Nutritional Assessment and Follow-Up*

All patients had a complete pre-therapy consultation with a dietician followed by weekly nutritional reviews while on therapy. Following therapy, dietetic review, whether by phone or in person, was conducted at least every two weeks following therapy until cessation of enteral feeding.

Adequacy of Enteral Intake (AEI) was recorded at each review using the scale: AEI 0 = 0–24%, AEI 1 = 25–49%, AEI 2 = 50–74% and AEI 3 = 75–100% of daily nutritional needs. All patients were followed until their AEI was less than 1.

Speech pathology services were offered to all patients with oropharyngeal dysphagia to minimize aspiration and malnutrition risk. Video fluoroscopy and Fibreoptic Endoscopic Evaluation of Swallowing were available for at-risk patients. Swallowing rehabilitation was not available to this patient cohort.

*Statistical Analyses*

Outcomes measured were 1) the risk of FT use for at least 25% of nutritional requirements (AEI ≥ 1) and 2) the duration of such use measured in days from the first date the AEI was recorded at 1 or higher to the date when it dropped to AEI 0 or the tube was removed.

Potential patient and tumor related prognostic variables were subdivided according to previously reported cut-off points.[16-19] Only variables which would be known at the pre-therapy multidisciplinary tumor board were considered. For analysis of risk of FT use (Yes or No) we used the Fisher exact test if there were only two subgroups (eg. age ≤ or > 65 years), the Cochran-Armitage test for trend if there were three or more ordered subgroups (eg. ECOG performance status) or the Pearson chi square test for three or more

unordered subgroups (eg. cancer site).[20] For analysis of duration of FT use, Kaplan-Meier analysis was carried out and subgroups were compared using the Mantel-Cox log rank test for differences or the Tarone-Ware test for trend.[21,22] As all patients were followed up to cessation of AEI ≥ 1 tube feeding, no durations were censored. All P values reported were two-sided and 95% confidence intervals (CI) were calculated. The significance criterion was $P < 0.05$ for previously reported prognostic factors or $P < 0.005$ for new prognostic factors (to adjust for multiple hypotheses).

Prognostic factors which were significant in the univariate analyses were tested in multivariable models to find the smallest number of independent prognostic factors which had a significant effect on the risk and duration of FT use. For risk of FT use, exact logistic regression with conditional maximum likelihood inference was used for the multivariable analyses with P values obtained from the exact conditional scores test.[20] For duration of FT use, Cox proportional hazards regression was used and the exponentials of the coefficients ($e^{\beta}$) from the final model were interpreted as "Recovery rate ratios".

Both backwards and forwards stepwise regression was performed and variables were retained in the model if the P value was < 0.05. Patients with unknown values for a particular factor were omitted from any models containing that factor, except for Human Papilloma Virus (HPV) where "unknown" was treated as a separate level of the factor.

**Results**

Between January 2007 and December 2013, 139 eligible patients were treated with radical intent IMRT. Their median age at commencement of RT was 61 years (range 20 to 91) and 78% were male. The most common cancer site was oropharynx (78 patients, 56%). The other primary sites were nasopharynx (16, 12%), supraglottis (15, 11%), glottic larynx (14, 10%), hypopharynx (5, 4%), oral cavity, (2, 1%) and unknown primary (9, 7%). Forty-one of the 78 oropharynx patients (53%) and five of the nine with unknown primaries (56%) had known HPV positive disease. Patient demographic and tumor characteristics are shown in the "Total" column in Table 1.

Altogether, 101 patients (73%) used a FT for at least 25% of their nutritional requirements, for at least 48 hours. The Kaplan-Meier curve of duration of FT use at AEI ≥ 1 is shown in Figure 1. Patients who did not use the FT at this level are represented in the Figure with 0 days duration; hence the curve starts at 73% on the vertical axis. The median duration of FT use for all patients was 70 days (CI 55–81 days). Twenty-four patients (17%) used it for at least six months, ten (7%) for at least 12 months and two (1%) for more than two years but the curve was curtailed at 24 months for the purpose of clarity.

Ninety patients (65%) used the FT for at least 75% of their requirements (AEI 3) at some stage and 18 (13%) used it at this level for more than six months.

Univariate analyses

Results of the univariate analyses on all 139 patients are shown in Table 1. Patients with cancer of the oral cavity or pharynx needed a feeding tube for longer than patients with cancers of supraglottis, glottic larynx or unknown primary (Figure 2). The other statistically significant prognostic factors for risk and duration of FT use were T-classification, N-classification, level 2 lymphadenopathy, bilateral neck lymphadenopathy, concurrent chemotherapy, prior dysphagia and prior malnutrition. BMI < 18.5 and negative HPV status in oropharynx or unknown primary patients were significantly associated only with longer duration of FT use. Retropharyngeal and level 3 nodal disease were not considered to be statistically significant factors, despite having P values less than 0.05, because they did not meet our criterion of $P < 0.005$ for new hypotheses and either risk or duration of FT use was not significant. Patients older than 65 years were less likely to use the FT than younger patients, yet there was no significant difference in duration of FT use. This was contrary to most previous studies. There were no significant associations between the risk or duration of tube feeding and tobacco or alcohol use, comorbidities scaled using the Charlson co-morbidity index, ECOG performance status, or levels 1, 4 or 5 lymphadenopathy.

Multivariable analyses

Cancer site was a significant prognostic factor, therefore, nine patients with unknown primaries were excluded from the multivariable analyses. Only one of the fourteen patients with glottic larynx cancer

needed to use a FT, so these patients were considered to be very low risk and also excluded from the multivariable analyses.

The remaining 116 patients with cancers in the pharynx, oral cavity or supraglottis were included in multivariable analyses for risk and duration of FT use for at least 25% of dietary needs. Factors with more than two subgroups were collapsed into two, specifically cancer site (pharynx and oral cavity versus supraglottis), T-classification (T3–4 versus T<3) and N-classification (N1–3 versus N0).

In the final models T-classification 3–4 (P = 0.0018 and P <0.0001 respectively) and level 2 nodal disease (P = 0.0030 and P = 0.0001 respectively) were the only independent significant predictors of risk and duration of FT use respectively (Table 2). The recovery rate (rate of ceasing FT use at AEI ≥ 1) with T3–4 disease was estimated to be 25% of the rate in patients with T<3 disease (CI 16% – 39%) and with level 2 nodal disease it was estimated to be 45% of the rate in patients with no level 2 nodes involved (CI 30% – 67%). Patients with both T-classification 3–4 and level 2 nodal disease were predicted to recover at approximately 11% of the rate of patients with neither factor (i.e. T<3 and no level 2 nodal disease) (CI 5% – 26%). Table 3 and Figure 3 display the observed duration of FT use in the presence of neither, one or both of these two significant factors.

None of the other factors, which were significant in the univariate analyses, was statistically significant in the multivariable analyses after taking into account T-classification 3–4 and level 2 lymphadenopathy.

**Discussion**

This analysis introduces a clinically useful and simple screening tool for both risk and duration of significant FT use, which is relevant when IMRT is used. Stratifying pharynx, oral cavity and supraglottis patients by two variables – T-classification (3–4) and presence of involved level 2 lymph nodes – separates patients into four distinct groups. Low risk patients have neither risk factor, low–intermediate risk patients have T<3 tumors with level 2 lymph nodes involved, high-intermediate risk patients have T3–4 tumors without level 2 nodes and high risk patients have T3–4 tumors and level 2 lymphadenopathy. This information is readily available when a patient is first presented at a Multidisciplinary Tumor Board and the model described

could be used to guide decisions regarding insertion of prophylactic tubes. It does not take dosimetric factors into consideration.

In our experience, all but the lowest risk group had at least an 85% chance of requiring enteral feeding for at least 25% of their diet, for at least 48 hours, at some stage during therapy or convalescence. Patients with glottic larynx cancer had a very low risk of needing a feeding tube (approximately 7% in our limited data). The risk for patients with unknown primaries in the head and neck is likely to depend on the volume of pharyngeal mucosa and constrictor muscles irradiated and whether patients had level 2 nodal involvement. These patients received elective mucosal irradiation, predominantly base of tongue and tonsillar fossae, to 63Gy and often concurrent chemotherapy, but did not suffer physical obstruction from macroscopic tumor.

There still remains substantial controversy as to whether patients are best managed via reactive or prophylactic FT for RT related dysphagia.[11] However, even departments that adhere to strict reactive FT protocols insert prophylactic tubes in a subset of high risk patients, and, conversely, departments with policies of liberal prophylactic FT use will choose to spare a low risk subset of patients from undergoing the insertion procedure.

Apart from cancer site, we found advanced T-classification to be the most significant prognostic factor for duration of FT use. This is not a new finding and is consistent with the observations of numerous published studies.[16, 23-26] The most common dichotomy of T-classification in the published literature has been T1–2 versus T3–4 with the more advanced classifications universally having higher rates of acute and long term FT use.[16, 26, 27] The findings of our study support this.

The impact of level 2 lymph nodes on patient dysphagia is a novel finding. Lymph node positivity has been associated with increased FT dependence at six months (OR 7.08; $P < 0.001$).[26] We are able to report specifically on this subset of node positive patients owing to the careful and consistent target delineation under the direction of a single radiation oncologist. The causality of this finding remains unclear. Level 2 lymph nodes have a strong association with primary cancers of the oropharynx and, in the current series,

69% of both oropharynx and nasopharynx cancers had level 2 adenopathy.[28] Numerous studies have shown that radiotherapy for oropharynx malignancy is associated with high rates of symptomatic dysphagia.[16, 26,29, 30] In this study, all patients with oropharyngeal and nasopharyngeal cancer had elective, bilateral irradiation of neck level 1B. This would lead to high dose deposition in the region of the patient's submandibular glands, which has been documented to increase the risk of both xerostomia and dysphagia.[26, 31] Anatomically, level 2 nodes are close to the parotid glands. Like the submandibular glands, the risk and severity of both xerostomia and dysphagia have been associated with increasing dose to parotid glands.[32-34, 35]The level 2 region lies lateral to the base of tongue for its entire cranio-caudal length.[15] The tongue base has been described as a crucial organ in swallowing and an increasing risk of dysphagia has been documented with increasing dose to this organ.[26]

Level 2 node involvement is associated with more advanced disease and thus more aggressive therapy, such as altered fractionation or use of concurrent systemic therapy. However, this is only by virtue of node positivity and a similar relationship was not seen in this study with adenopathy at other stations.

Regarding our univariate analysis, the finding that patients with pharyngeal and oral cavity carcinomas suffered more dysphagia than those with laryngeal primaries has been previously well documented.[26] Our finding that older patients were less likely to use FT is consistent with that of Wopken et al but is inconsistent with other published studies.[25, 26, 36] We did not observe any effect of alcohol abuse on FT use, as seen by Frowen et al.[24]

The results of this study differ from several others in the duration of FT use for at least 25% of dietary needs. The median duration was over two months and at six months, 17% percent of patients were still using their FT. While earlier series have reported significantly higher rates of prolonged FT use, many modern studies, that have included patients treated with IMRT, have cited lower rates of long-term FT .[5, 11, 26, 35-38]

It is important to distinguish FT use from FT dependence. A proportion of patients in this study who were using their FT at six months were also taking food and supplements orally. Eighteen patients (13%) were using their FT for more than 75% of daily needs for more than six months, which is consistent with recently

published prophylactic cohorts, such as Wopken et al (10.7%). Regardless of nutritional intervention, it is common for patients with head and neck cancer to lose more than 10% of their bodyweight during and immediately following therapy .[2, 3] In many cases, an in situ gastrostomy tube provides a convenient way to optimize patient nutrition, even when they are eating. These patients have already avoided or suffered the potential complications associated with gastrostomy insertion, so it is not surprising that dieticians and nutritional counsellors sometimes encourage ongoing nutritional supplementation in patients still eating.

In the short term, gastrostomies are more comfortable and convenient than nasogastric tubes and have less negative impact on body image and family life.[12] For this reason, it is not surprising that the medical literature almost universally reflects longer duration of FT use with gastrostomy as opposed to reactive nasogastric tubes.[12, 39-41] In reports where FT use at six months is less than 5%, a nasogastric tube was inserted as a reaction to failure of oral nutrition. It is not surprising that nasogastric tubes were not kept in-situ or repeatedly re-inserted for the purpose of nutritional optimisation, given the poor acceptability of this FT on body image psychosocial function.[11, 12, 38, 42]

Undoubtedly, long term FT dependence has a striking negative impact on many domains of quality of life.[43-47] A considerable amount of published data suggests that patients with prophylactic FT's are less likely to maintain an oral, or partial oral, diet during RT and that this can negatively affect short and long-term diet outcomes, as well as duration of FT dependence.[11, 48, 49] Despite the majority of reported studies showing higher FT use at six months with prophylactic FT, Salas et al found no difference and Silander et al reported lower rates of grade 3 dysphagia in patients with a prophylactic gastrostomy tube (2% vs 9%).[40, 50]

The high risk and duration of FT use in this study can also be explained by the high risk patients enrolled. All patients had bilateral neck irradiation, and gross disease was treated to an equivalent dose of 70Gy. Many series have included patients who were treated with ipsilateral and postoperative RT, who are not expected to use FTs routinely. In this series, 84 patients were treated with concurrent systemic therapy. This is known to increase acute toxicity, including severe dysphagia, although it did not affect FT use in our series.[51] Whilst concurrent chemotherapy did not retain significance following multivariable analyses, there may be some co-linearity with both T- and N-classification and the role it plays in more advanced disease.

Tumors of the glottic larynx had low risk of FT dependence and were excluded from the multivariable regression analyses. While earlier studies by Eisbruch, Caudell and Caglar have shown the larynx to be an important RT avoidance structure, a recent study by Wopken shows that patients with laryngeal primaries are the least likely to suffer FT dependence at six months (OR 1.00 vs. 13.82 for oropharynx and 16.19 for hypopharynx; $p<0.001$).[26, 36, 52-54] Treatment of salivary gland tumors is very rarely associated with dysphagia and therefore, this patient cohort was not included in this study.

In this study, no patient had access to swallowing rehabilitation. A randomized controlled trial reported by Carnaby-Mann et al. showed that swallowing exercises led to less deterioration of swallowing muscles and functional swallowing ability during chemoradiotherapy for head and neck cancers.[14] Patients randomised to swallowing exercises were more likely to maintain an oral diet and were less likely to use a FT.[14] Hutcheson et al. reported that adherence to swallowing exercises was similarly effective to maintenance of an oral, or partial oral, diet during chemoradiotherapy for better long term diet and shorter FT use.[49] The lack of swallowing exercises in this study may limit the ability the applicability of our data to patients who are exercising. However, the complete absence of swallowing exercises in this cohort, contributes to the uniformity of our data and possibly the internal validity of our findings. Swallowing exercises have definite patient benefits, but not all patients are adherent to prescribed swallowing exercises and many patients are partially adherent, making these benefits difficult to quantify.[14,49]

Furthermore, every effort was made to minimize patient pain, as analgesia has been associated with a shorter duration of FT use.[47] All patients were reviewed at least weekly by a medical doctor to prescribe analgesia in a stepwise fashion: mouthwashes and anti-thrush measures, simple analgesia (e.g. soluble paracetamol), local anaesthetic mouthwashes (e.g. xylocaine and cocaine), and ultimately titration of opioids. Prophylactic gabapentin was not administered, as it is not registered for this use in Australia, though it has been associated with reduced FT use in a previously published study.[47]

This study possesses all the limitations inherent to a single-institution, retrospective analysis. We are unable to provide data on patients' functional swallowing ability, however, we are able to accurately report on patients having oral, or partial oral, diet at various time points due to comprehensive, prospectively

recorded nutritional data. All of the patients were treated by a single radiation oncologist, however, it must be acknowledged that these patients were treated over eight years, a sufficient time period for even individual practice to vary. All patients were treated in the FDG PET and IMRT era, without swallowing exercises. This lends to uniformity in staging, volume delineation, and treatment delivery across the cohort. This study proposes a simple and novel clinical risk stratification tool that warrants prospective validation.

**Conclusion**

In patients with pharynx or supraglottic larynx cancers treated with definitive, bilateral IMRT, with or without concurrent systemic therapy, two clinical risk factors, namely T-classification 3–4 and level 2 lymphadenopathy, can potentially stratify patients into four distinct risk groups for developing severe dysphagia requiring FT use for at least 25% of their dietary requirements. This stratification may be useful in the clinic prior to radiotherapy planning and treatment so that patients at risk may have a FT inserted early prior to further nutritional status deterioration.

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Table 1. Univariate analyses of prognostic factors for feeding tube use (Yes/No) and duration in 139 patients

| Prognostic factor | Subgroup | Feeding tube used* | | | Days of feeding tube use* | | |
|---|---|---|---|---|---|---|---|
| | | Yes/Total | % | P value† | Median | (95% CI) | P value‡ |
| Cancer site | Pharynx or oral cavity | 86/101 | 85% | < 0.0001 | 89 | (70 – 120) | < 0.0001 |
| | Larynx, supraglottis | 10/15 | 67% | | 16 | (0 – 79) | |
| | Larynx, glottis | 1/14 | 7% | | 0 | (0 – 0) | |
| | Unknown primary | 4/9 | 44% | | 0 | (0 – 66) | |
| Human papilloma virus (HPV) | Negative | 22/23 | 96% | 0.13 | 163 | (81 – 233) | 0.004 |
| (for 87 oropharynx/unknown 1°) | Positive | 35/46 | 76% | | 61 | (31 – 90) | |
| | Unknown | 13/18 | 72% | | 59 | (0 – 77) | |
| T stage | X, 0 | 4/10 | 40% | 0.0007 | 0 | (0 – 66) | < 0.001 |
| | 1 | 15/23 | 65% | | 50 | (0 – 77) | |
| | 2 | 31/47 | 66% | | 44 | (7 – 75) | |
| | 3 | 34/40 | 85% | | 119 | (79 – 173) | |
| | 4 | 17/19 | 89% | | 150 | (57 – 262) | |
| N stage | 0 | 22/44 | 50% | 0.0004 | 7 | (0 – 59) | 0.006 |
| | 1 | 16/20 | 80% | | 75 | (44 – 120) | |
| | 2 | 60/70 | 86% | | 86 | (70 – 122) | |
| | 3 | 3/5 | 60% | | 45 | (0 – >295) | |
| Bilateral neck node disease | No | 70/104 | 67% | 0.016 | 59 | (28 – 75) | 0.025 |
| | Yes | 31/35 | 89% | | 118 | (57 – 170) | |
| Retropharyngeal node disease | No | 93/131 | 71% | 0.11 | 66 | (50 – 79) | 0.025 |
| | Yes | 8/8 | 100% | | 153 | (14 – >834) | |
| Level 1 node disease | No | 85/120 | 71% | 0.28 | 70 | (57 – 83) | 0.58 |
| | Yes | 16/19 | 84% | | 55 | (18 – 113) | |
| Level 2 node disease | No | 36/62 | 58% | 0.0010 | 37 | (0 – 68) | 0.0054 |
| | Yes | 65/77 | 84% | | 83 | (65 – 120) | |
| Level 3 node disease | No | 72/107 | 67% | 0.012 | 65 | (31 – 79) | 0.53 |
| | Yes | 29/32 | 91% | | 86 | (57 – 136) | |
| Level 4 node disease | No | 90/127 | 71% | 0.18 | 68 | (49 – 79) | 0.14 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Yes | 11/12 | 92% | | 124 | (45 – 393) | |
| Level 5 node disease | No | 92/128 | 72% | 0.73 | 70 | (49 – 81) | 0.55 |
| | Yes | 9/11 | 82% | | 58 | (0 – 393) | |
| Concurrent chemotherapy | No | 30/55 | 55% | 0.0002 | 16 | (0 – 59) | 0.0048 |
| | Yes | 71/84 | 85% | | 86 | (75 – 118) | |
| Dysphagia or odynophagia | No | 75/110 | 68% | 0.020 | 59 | (42 – 77) | 0.009 |
| | Yes | 26/29 | 90% | | 133 | (70 – 200) | |
| Nutrition (PG-SGA) | Well-nourished | 72/106 | 68% | 0.012 | 58 | (42 – 75) | 0.001 |
| (1 missing) | Malnourished | 29/32 | 91% | | 147 | (77 – 211) | |
| Body Mass Index | Underweight (<18.5) | 10/12 | 83% | 0.51 | 208 | (81 – 479) | 0.002 |
| (15 missing) | Not underweight (≥18.5) | 80/112 | 71% | | 65 | (45 – 77) | |
| Age on commencing RT | ≤ 65 years | 70/88 | 80% | 0.019 | 75 | (58 – 90) | 0.74 |
| | > 65 years | 31/51 | 61% | | 31 | (0 – 106) | |
| ECOG Performance Status | 0 | 43/58 | 74% | 0.87 | 58 | (35 – 79) | 0.17 |
| | 1 | 53/74 | 72% | | 70 | (50 – 116) | |
| | 2 | 5/7 | 71% | | 128 | (0 – >303) | |
| Charlson Comorbidity Index | 0 | 55/72 | 76% | 0.23 | 70 | (45 – 101) | 0.85 |
| | 1 | 16/22 | 73% | | 59 | (10 – 108) | |
| | 2 | 19/27 | 70% | | 77 | (16 – 170) | |
| | 3, 4, 5 | 11/18 | 61% | | 17 | (0 – 136) | |
| Tobacco smoking | Never or minimal | 39/46 | 85% | 0.13 | 70 | (50 – 101) | 0.53 |
| (4 missing) | Past | 27/42 | 64% | | 55 | (0 – 90) | |
| | Current | 33/47 | 70% | | 70 | (42 – 128) | |
| Alcohol drinker | Never or social | 69/94 | 73% | 0.73 | 66 | (44 – 90) | 0.46 |
| (5 missing) | Past | 8/11 | 73% | | 120 | (0 – 200) | |
| | Current | 20/29 | 69% | | 57 | (14 – 77) | |

* "Feeding tube use" means feeding tube was used for at least 25% of nutritional requirements.

† Two-sided P value from Fisher exact test for difference between 2 subgroups, Pearson chi square test for difference between 3 or more unordered subgroups, or Cochran-Armitage test for trend across 3 or more ordered subgroups.

‡ Two-sided P value from Mantel-Cox log rank test for differences between subgroups or Tarone-Ware test for trend across 3 or more ordered subgroups.

Table 2. Final multivariable models for feeding tube use (Yes/No) and duration (n = 116) *

Feeding tube use (exact logistic regression with conditional maximum likelihood inference) †

| | | | | | Odds ratio | | Exact |
|---|---|---|---|---|---|---|---|
| Factor | Reference | Level | β | $s.e._{\beta}$ | OR | 95% CI | P value |
| T stage | T0–T2 | T3–T4 | 1.867 | 0·633 | 6.47 | 1·73–31.4 | 0·0018 |
| Level 2 nodes | No | Yes | 1.640 | 0·559 | 5.15 | 1·56–19.0 | 0·0030 |

Duration of feeding tube use (Cox proportional hazards regression) †

| | | | | | Recovery ratio | | Exact |
|---|---|---|---|---|---|---|---|
| Factor | Reference | Level | β | $s.e._{\beta}$ | RR | 95% CI | P value |
| T stage | T0–T2 | T3–T4 | -1.388 | 0·230 | 0.25 | 0.16–0.39 | <0·0001 |
| Level 2 nodes | No | Yes | -0.795 | 0·205 | 0.45 | 0.30–0.67 | 0·0001 |

* "Feeding tube use" means feeding tube was used for at least 25% of nutritional requirements.

† β = coefficient for each Level relative to the Reference category, based on 116 patients with cancers of pharynx, oral cavity or supraglottis. $s.e._{\beta}$ = estimated standard error of β. OR or RR = $e^{\beta}$. 95% CI = 95% confidence interval for the OR or RR = $e^{\beta \pm 1{\cdot}96\ (s.e.\beta)}$.

‡ Other factors which were not significant when added individually to the models were: body mass index (<18.5 vs ≥18.5), nutrition (PG-SGA mal-nourished vs well nourished), dysphagia (Yes vs No), cancer (pharynx/oral cavity vs supraglottic larynx), human papilloma virus status (positive/unknown vs negative), N stage (N1–3 vs N0), bilateral neck nodes (Yes vs No), and planned concurrent chemotherapy. When added individually to the above models, the P values for these factors were all >0.3 for incidence and >0.1 for duration of feeding tube use.

Table 3. Prognostic groups based on T stage and Level 2 lymphadenopathy: data from 116 patients with cancers of pharynx, oral cavity or supraglottis.

| | | | Feeding tube used* | | | Days of feeding tube use* | |
|---|---|---|---|---|---|---|---|
| **Group** | **T stage** | **Level 2 nodal disease** | **Yes/Total** | **%** | **(95% CI)** | **Median** | **(95% CI)** |
| 1 | T0–2 | No | 10/20 | 50% | (27 – 73) | 7 | (0 – 59) |
| 2 | | Yes | 36/42 | 86% | (70 – 95) | 75 | (56 – 90) |
| 3 | T3–4 | No | 24/27 | 89% | (71 – 98) | 108 | (68 – 173) |
| 4 | | Yes | 26/27 | 96% | (81 – 100) | 170 | (113 – 295) |
| All pharynx, oral cavity, supraglottis patients | | | 96/116 | 83% | (75 – 89) | 79 | (68 – 106) |

* "Feeding tube use" means feeding tube was used for at least 25% of nutritional requirements.

Figure 1. Duration of feeding tube use for at least 25% of nutritional requirements for all 139 patients. Kaplan-Meier analysis.

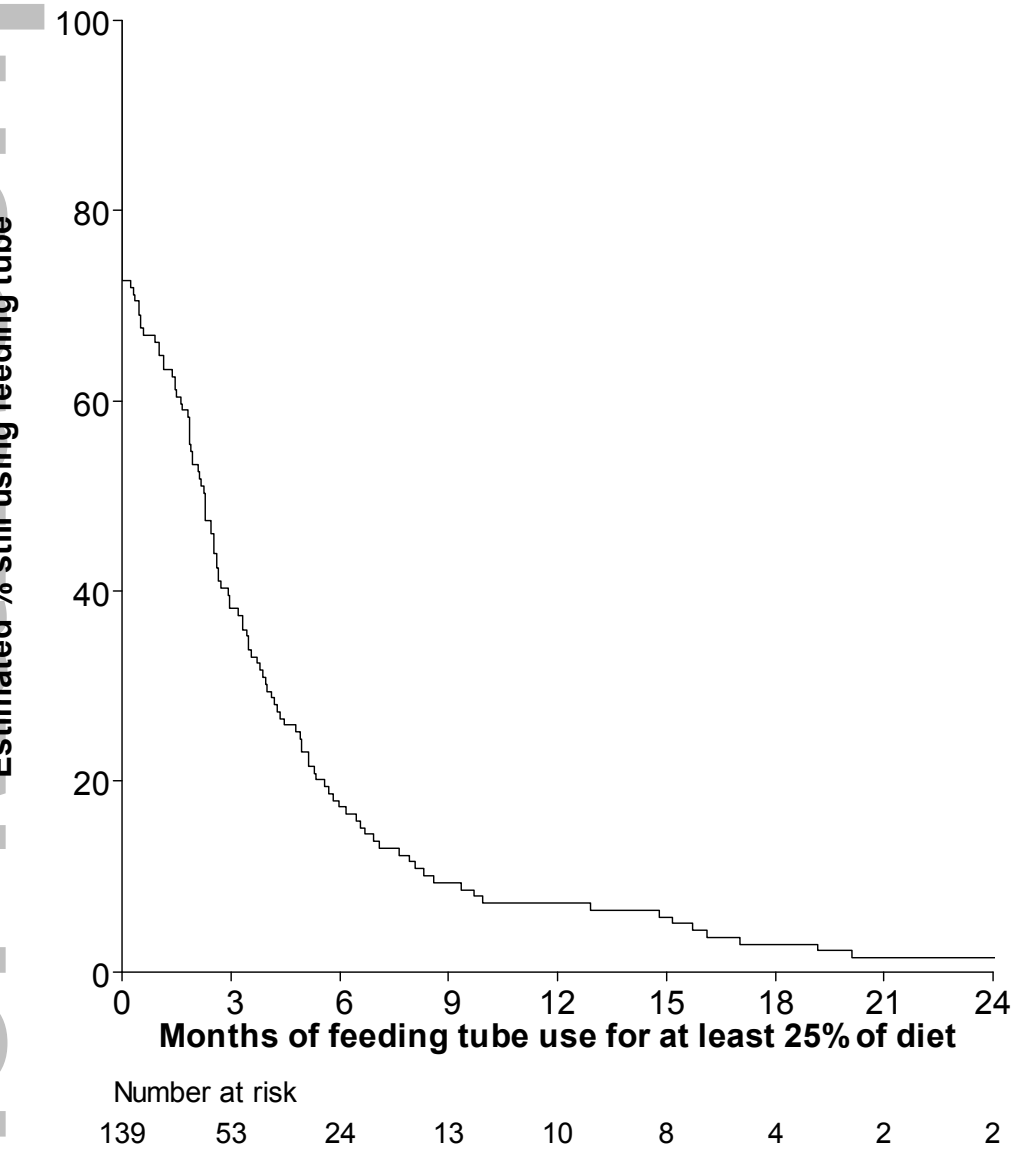
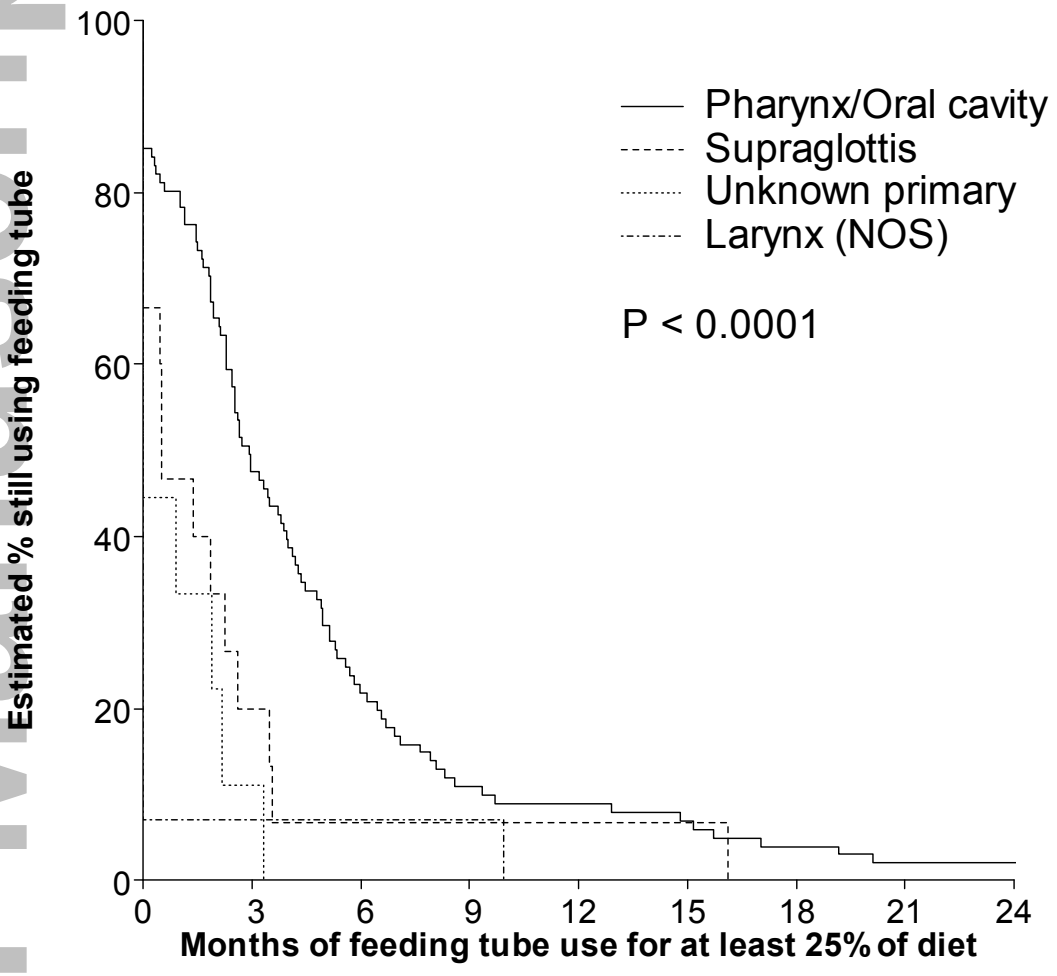
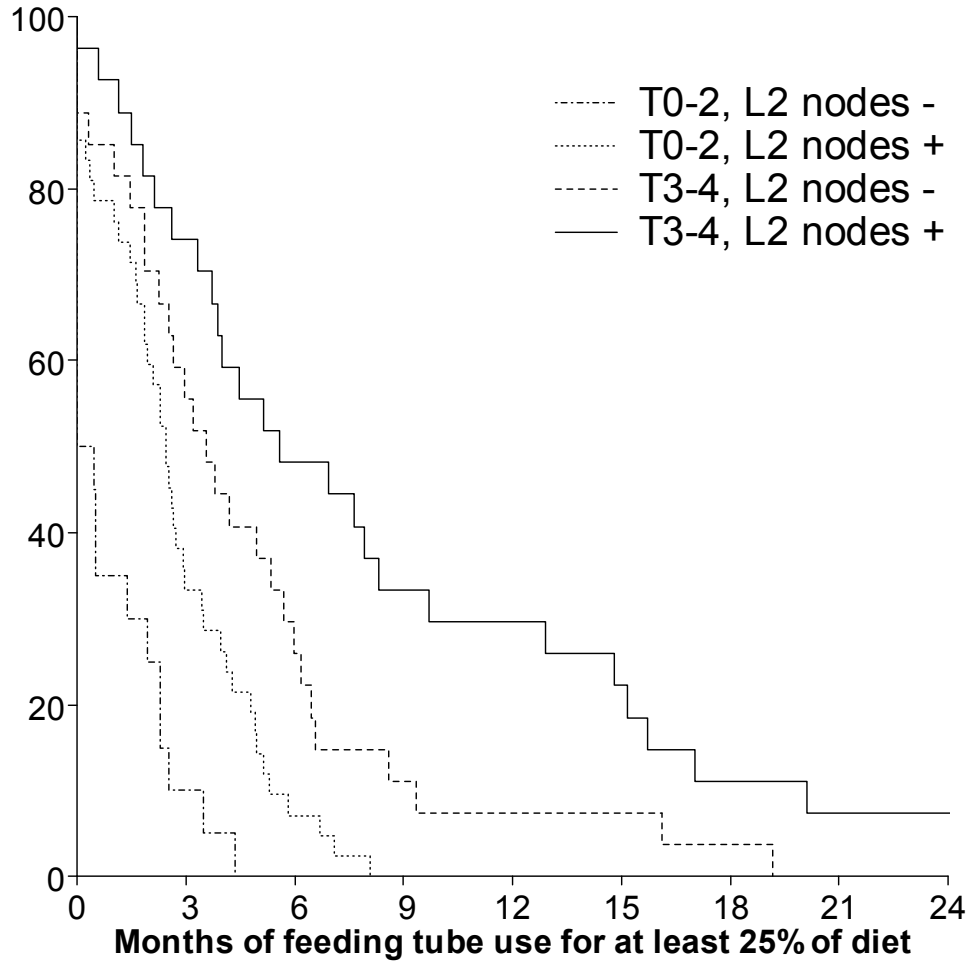


Figure 2 Duration of feeding tube use for at least 25% of nutritional requirements by primary cancer site. Kaplan-Meier analysis, 139 patients.




| Number at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Pharynx/OC | 101 | 48 | 22 | 11 | 9 | 7 | 4 | 2 | 2 |
| Supraglottis | 15 | 3 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| Unknown | 9 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Larynx (NOS) | 14 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |

Figure 3 Duration of feeding tube use for at least 25% of nutritional requirements by prognostic group according to T-stage and level 2 lymphadenopathy. Kaplan-Meier analysis, 116 patients with pharynx, oral cavity or supraglottis cancers.




Number at risk

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| T0-2, L2 - | 20 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| T0-2, L2 + | 42 | 14 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| T3-4, L2 - | 27 | 15 | 7 | 3 | 2 | 2 | 1 | 0 | 0 |
| T3-4, L2 + | 27 | 20 | 13 | 9 | 8 | 6 | 3 | 2 | 2 |

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