RESEARCH ARTICLE

Comparison of Treatment Compliance and Nutritional Outcomes among Patients with Nasopharyngeal Carcinoma with and without Percutaneous Endoscopic Gastrostomy during Chemoradiation

Thanarpan Peerawong[1]*, Temsak Phungrassami[1], Kovit Pruegsanusak[2], Rassamee Sangthong[3]

Abstract

Aims: The study aimed to compare treatment compliance and nutritional outcomes in nasopharyngeal carcinoma (NPC) patients during chemoradiation. Methods: Clinical information of patients with NPC that underwent chemoradiation during 2004-2009 were retrieved from the hospital database and retrospectively reviewed. Patients were categorised into a prophylactic percutaneous endoscopic gastrostomy (PPEG) group and a non-PPEG group. Clinical information including treatment compliance, weight, haematological and renal toxicity was compared. Results: A total of 219 patients were reviewed and categorised into PPEG (n=77) and non-PPEG (n=142). Significant differences in absolute percentage weight loss between groups were found from the 3rd cycle of chemotherapy. There were 24.2, 20.3 and 24.8% in the third, the fourth and the fifth cycles of chemotherapy, respectively. Migration of grade 2 to grade 3 weight loss was obviously seen in the 3rd cycle as well. A significant difference of grade 3 or more hypokalemia was found with values of 14.3% and 50% in the PPEG and non-PPEG groups, respectively. Other toxicity parameters and treatment compliance were not different between the groups. Conclusions: Use of PPEG resulted in decreased severe weight loss, reduced migration from grade 2 to grade 3 weight loss and reduced hypokalaemia. However, benefits in treatment compliance could not be detected. So consideration of PPEG in NPC patients requires care.

Keywords: Prophylactic percutaneous endoscopic gastrostomy - nasopharyngeal carcinoma - weight loss

Asian Pacific J Cancer Prev, **13 (11)**, 5805-5809

Introduction

Weight loss is a common problem in patients with head and neck cancer that contributes to impaired treatment tolerance, poor quality of life and shortened survival time of the patients (Capuano et al., 2008; 2010; Datema et al., 2011). A systematic review found that the average weight reduction among head and neck patients during treatment was about 2.3-8 kg (Paleri and Patterson, 2010). Weight loss in patients with nasopharyngeal carcinoma was more severe with an average weight reduction of 5.5-12.3 kg and 86% of patients experienced more than 10% weight loss due to chemoradiation (Bahl et al., 2004).

Current standard treatments of locally advanced head and neck cancers are surgery followed with radiotherapy or chemoradiotherapy for patient whom had positive margin or extracapsular extension. The role of concurrent chemoradiotherapy as the main treatment is in the organ preservation or unresectable disease. The standard treatment schedule for head and neck cancer is the 3 cycles of cisplatin 100 mg/m^2 every 3-weeks concurrent with radiotherapy 70 Grey (Gy) in 35 Fraction (F) 5 F per week. But in the nasopharyngeal carcinoma treatment is unique. Radiotherapy is the main treatment that can cure the patient. The additional 6 cycles of chemotherapy, 3 cycles concurrent with radiotherapy and followed with 3 cycles adjuvant as proposed by Al-Sarraf et al. improve 3-year progression-free survival and overall survival (Al-Sarraf et al., 1998).

During therapy, patients may suffer from many acute complications such as mucositis, dysphagia, nausea, and vomiting. These symptoms could lead them to dehydration, undernutrition, and eventually worsens the treatment outcome. Therefore nutritional status improvement is an important key to maintaining patients' treatment compliance during intensive treatment. Nourishment can be undertaken via percutaneous endoscopic gastrostomy and inserting the feeding tube to the stomach through the abdominal wall before radiation, called "prophylactic percutaneous endoscopic gastrostomy" (PPEG). PPEG has been effective in the maintenance of weight, reduced set-up error, reduced hospitalisation, reduced treatment

*[1]Department of Radiology, [2]Department of Otolaryngology Head and Neck Surgery, [3]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand *For correspondence: pthanarpan@gmail.com*

interruption and improved quality of life (Lee et al., 1998; Chang et al., 2009; Mercuri et al., 2009; Salas et al., 2009; Chen et al., 2010; Assenat et al., 2011; Silander et al., 2011).

The evidence of PPEG for improved nutritional status is limited in head and neck non-nasopharyngeal carcinoma patients. Nasopharyngeal carcinoma is a subset of cancer in this area, with differences in natural history and treatment regimens were blended in with the studies. The number of nasopharyngeal carcinoma patients in these studies were 23%, 15% and 1.5% in Chen et al. (2009) Mercuri et al. (2010) and Silander et al. (2011)'s studies, respectively. These results may not fit nasopharyngeal carcinoma because the chemotherapy regimen and target volume of radiation are different. So the effect of PPEG in preventing weight loss in Nasopharyngeal carcinoma is still in question.

This study aims to examine nutritional outcomes, toxicities and compliance during treatment among patients with nasopharyngeal carcinomas who underwent concurrent chemoradiation.

Materials and Methods

Study design

The Ethics Committee of the Faculty of Medicine, Prince of Songkla University, has approved this study. All patients with nasopharyngeal carcinoma who received chemoradiation at Songklanagarind Hospital during January 2004 – December 2009 were retrieved from the hospital database. Inclusion criteria for retrospective review were patients with stage IIb - IVb squamous cell carcinoma according to AJCC/TNM 6th edition (2002); age above 18 years; had Eastern Cooperative Oncology Group (ECOG) score ≤2. The patients were excluded if they had metastasis, received a weekly dose of carboplatin, were treated with altered fractionation schedule (AF) or used the intensity modulated radiotherapy technique (IMRT).

Data on age, gender, comorbidities, initial weight, ECOG, TNM staging and chemotherapy regimens were recorded before starting treatment. Weight in kg was recorded at baseline and subsequent chemotherapy sessions. The blood tests for evaluation of the treatment toxicities were recorded at the baseline and in subsequent sessions of chemotherapy. The haematological toxicities were evaluated with white blood cell counts (WBC) and haemoglobin levels (Hb). Renal toxicity was examined by renal function estimated by creatinine clearance with the Cockcroft-Gault formula (Gault et al., 1992). Levels of sodium and potassium were evaluated using electrolyte statuses. The above parameters were classified by following Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 (http://ctep.cancer.gov) and divided into patients who experienced toxicities grades 1-2 and grade 3-5

The compliance of treatment was divided to radiotherapy and chemotherapy compliances. The radiotherapy compliance was the number of patients who completed the radiation schedule, radiation dose and duration from the start to the end of treatment. Chemotherapy compliance was the number of patients who completed chemotherapy treatment.

Treatment regimen

Conventional radiation or three-dimensional radiotherapy technique was performed with the total radiation dose of 70 Gy in 35 F, 5 F per week and 50 Gy in 25 F, 5 F per week for gross and microscopic tumour, respectively. Treatment was delivered by a cobalt machine or 6-MV linear accelerators (C0-60 phoenix P56, Clinac 6EX and Clinac 2100C). A total of five cycles of chemotherapy were given, following the protocol of the institute. Cisplatin 100 mg/m^2 or carboplatin AUC6 was given every 3 weeks for 3 cycles in the concurrent phase. After completed radiation, an additional 2 cycles of cisplatin 75-80 mg/m^2 or carboplatin AUC5 on day 1 and 5-FU 1,000 mg/m^2 on day 1-4 every, 4 weeks were administered. Doses of chemotherapy given were adjusted based on patients' haematological results and renal toxicity.

During treatment, patients visited the radiation oncology clinic weekly and otolaryngology clinic every three weeks during concurrent phase and monthly during adjuvant chemotherapy phase. Patients were evaluated at both clinics for treatment toxicities and support. The otolaryngologists gave the chemotherapy. The patients would be admitted if they developed fatigue, electrolyte imbalance or infection, which needed intravenous treatment. The clinical parameters including body weight, complete blood count, renal function and electrolyte levels were recorded in the computerized hospital information system.

Statistical analysis

Descriptive statistics were used to describe clinical data. Weight change was defined as a difference in current weight from the baseline. The percentage of weight loss was defined by the percentage of weight change in each cycle of chemotherapy compared with their baseline weight and classified into grades1-3. Severe weight loss was defined as more than 10% weight loss from the baseline. Comparisons of continuous data were done by Student's t-test, for normal distributed data and a rank sum test for non-normal distributed data. Categorical data was compared by chi-squared test or Fisher's exact test. Statistical significant was defined at p-value <0.05. All statistical analysis was done by R program (Epicalc package) (R Foundation for Statistical Computing, 2008; Chongsuvivatwong, 2011).

Results

Subject characteristics

During 2004-2009, 247 patients were diagnosed of nasopharyngeal carcinoma. After initial review of medical records, 28 of them were excluded from the study. A total of 219 patients remained and were subsequently categorised into PPEG (n=77) and non-PPEG groups (n=142).

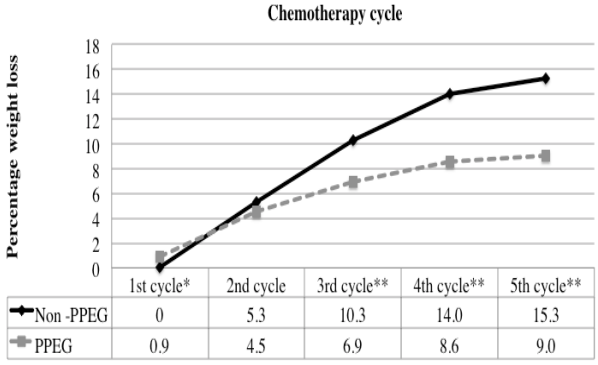
Baseline characteristics including age, sex, weight and tumor staging were not significantly different between the two groups. However, they had differences in ECOG

performance status and co-morbidities as shown in table1. The patients, who had ECOG=0, were found in 48.1% (n=37) and 28.2% (n=40) in PPEG groups and non-PPEG groups. But patients in PPEG groups had more comorbidity, 33.8% (n=26) and 13.8% (n=26). The patients with PPEG retained a tube for an average of 237 (181-294) days.

Weight loss

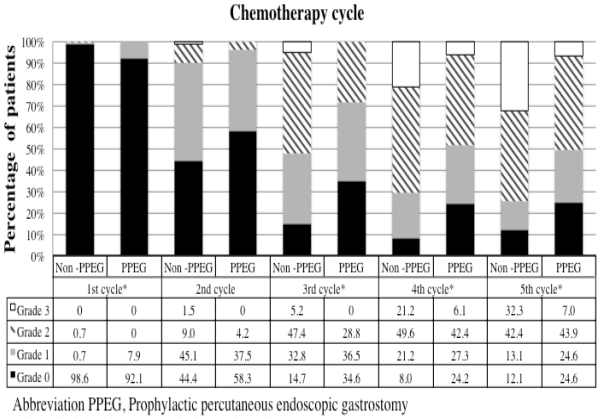
In the entire study, the percentage weight loss in each cycle of chemotherapy increased over the treatment period in both PPEG and non-PPEG groups. At the 1st cycle of the chemotherapy, patients with PPEG had weight loss of 0.9% (0-2.3%) while patients without PPEG had no weight change. The weight loss was not different between the groups in 2nd cycle of chemotherapy until the third cycle of chemotherapy, the patients without PPEG lost more weight (Figure 1). In the 3rd, 4th and 5th cycle of chemotherapy, the percentage of weight loss between the groups were significant. The absolute difference of percent weight loss was 3.4%, 5.4% and 6.3%, respectively.

Patients who developed severe weight loss increased over the treatment period (Table 2). The severe weight loss had developed since the 1st cycle of chemotherapy.



Abbreviation PPEG, Prophylactic percutaneous endoscopic gastrostomy
* Statistical significant was calculated with rank sum test
** Statistical significant was calculated with Student's *t*-test

Figure 1. Weight Loss (%) of Nasopharyngeal Carcinoma Patients between Non-PPEG and PPEG During a Chemotherapy Session



Abbreviation PPEG, Prophylactic percutaneous endoscopic gastrostomy
* Statistical significant was calculated with chi-squared test

Figure 2. The Percentage of Grade 0-3 Weight Losses in Nasopharyngeal Carcinoma Patients With and Without PPEG in Each Subsequent Session of Chemotherapy

There were 0.7% and none in non-PPEG group and PEG group. But the significant difference was found in the 3rd, 4th and 5th cycle of chemotherapy. The absolute difference between groups was 24.2%, 20.3% and 24.8%. Patients with severe weight loss were categorised into grade 2 and grade 3 by the toxicity criteria. The migration from grade 2 to grade 3 was found more in the non-PPEG group. The results were obviously seen in each cycle of chemotherapy. The absolute differences of grade 3 weight loss between both groups are 0, 1.5, 5.2, 15.2 and 25.3% in each cycle of chemotherapy. The significant difference was detected since the 3rd cycle as shown in Figure 2 as well.

Treatment toxicity

The haematological toxicities were evaluated in two aspects, leukocytopenia and anaemia. Grade 3 leukocytopenia was 24.4% and 16.7% in the non-PPEG and PPEG group. Grade 3 anaemia was 12% and 8.3% respectively. No significant differences were detected in haematological toxicities between the two groups.

The renal function, estimated creatinine clearance, of all patients was found in grade 1-2 toxicity. The electrolyte imbalances with grade 3 hyponatremia were 38.6% and 23.5% in the non-PPEG and PPEG group without statistical difference. The grade 3 hypokalemia was different between both groups showing 50% and 14.3% (p=0.002). In subgroup analysis, the advantages showed in the 4th and 5th cycle of chemotherapy. There were 7.6%,

Table 1. Demographic and Clinical Characteristics of Locally Advance Nasopharyngeal Carcinoma Patients (n=219) with PPEG (n=77) and without PPEG (n=142) Before Starting Treatment

Characteristics		Non-PPEG n (%)	PPEG n (%)	p-value
Age (year) (mean±SD)		48.7±12.3	50.7±11.1	0.23
Male		100 (70.4)	52 (67.5)	0.772
Comorbidity		26 (18.3)	26 (33.8)	0.016*
	Diabetes	4 (2.8)	5 (6.5)	0.284
	Hypertension	22 (15.5)	14 (18.2)	0.748
	Others	10 (7)	15 (19.5)	0.011*
Initial weight (Kg) (median (maximum, minimum))		60 (52.7,68.3)	56 (50.5,66)	0.15
ECOG	0	40 (28.2)	37 (48.1)	0.009*
	1	82 (57.7)	33 (42.9)	
	2	20 (14.1)	6 (7.8)	
Stage	T stage			
	T1	20 (14.1)	8 (10.4)	0.731
	T2	44 (38.1)	36 (46.8)	
	T3	22 (15.5)	11 (14.3)	
	T4	46 (32.4)	22 (28.6)	
	N stage			
	N0	6 (4.2)	4 (5.2)	0.964
	N1	35 (24.6)	20 (26)	
	N2	66 (46.5)	34 (44.2)	
	N3a	16 (11.3)	7 (9.1)	
	N3b	19 (13.4)	12 (15.6)	
Type of chemotherapy				
	Cisplatin	74 (52.1)	49 (63.6)	0.067
	Carboplatin	51 (35.9)	16 (20.8)	
	Both	17 (12.0)	12 (15.6)	

*Statistical significant was calculated with chi-squared test, PPEG, Prophylactic percutaneous endoscopic gastrostomy

Table 2. Number of Patients [n (%)] Who Developed Weight Loss, Greater Than 10% in Each Subsequent Treatment

Treatment schedule	Non-PPEG	PPEG	p-value
1st cycle	1 (0.7)	0 (0)	1
2nd cycle	14 (10.5)	3 (4.2)	0.19
3rd cycle	62 (53.0)	15 (28.8)	0.006*
4th cycle	81 (71.1)	32 (50.8)	0.004*
5th cycle	74 (74.0)	29 (49.2)	0.003*

*Statistical significant was calculated with chi-squared test, PPEG, Prophylactic percutaneous endoscopic gastrostomy

10.5% in the non-PPEG group and 0% and 1.7% in the PPEG group.

Treatment compliance

Regarding the compliance of radiation treatment, both groups showed no difference. The percentages of patients who completed treatment are 95% and 96% for the non-PPEG and PPEG group. The mean radiation dose was 70 Gy in both groups. Treatment time was 52 (49-57) and 51 (49-56) days respectively. The patients who completed chemotherapy were 71% and 79% for the non-PPEG group and PPEG group without statistical significance.

Discussion

In this study, PPEG insertion could reduce weight loss 6.3% (9% from baseline in PPEG group and 15.3% from baseline in non-PPEG group). In Chen et al. 'study, they reviewed 120 head and neck patient (28 patients were diagnosed with nasopharyngeal carcinoma). The PPEG insertion could reduce weight loss during radiation therapy. The weight losses were 8% from baseline in PPEG group and 14% from baseline in non-PPEG group (Chen et al., 2010). In Mercuri et al. 'study, they conducted prospective non randomised study for evaluated effect of PPEG on the set-up variations in head and neck cancer patient. The 20 head and neck cancer patients were included (3 patients were diagnosed with nasopharyngeal carcinoma). They found 4.9 and 11.0% of weight loss from baseline in PPEG group and non-PPEG group (Mercuri et al., 2009). But Silander et al. (2011) conducted a randomised control trial to evaluate the effect of PPEG on malnutrition and quality of life. They included 134 head and neck cancers, mainly oropharynx and oral cavity cancer. The effects of PPEG on weight loss during treatment period were 13.6% in non- group and 11.4% in PPEG group. In addition, all patients after starting the treatment period, including 1-year and 2-year follow-ups, were not different. So the effect of PPEG on long-term weight loss may be small or none. However, the study had only 1.5% of Nasopharyngeal carcinoma in the sample. So the randomised study that included only nasopharyngeal carcinoma should be investigated.

In our study, the patients with PPEG seem to lose less weight during the treatment period, 0.9% weight loss from baseline that contributed to 7.9% of patients migrating from grade 0-1, at the 1st cycle of chemotherapy. Although it seems to have statistical significance, this may not be significant in clinical practice, so the advantage of PPEG on weight loss showed a pronounced effect from the 3rd cycle of chemotherapy and was explicit during adjuvant chemotherapy. Causes: a gap of 3rd and 4th cycle, after completed radiation treatment, patients still experience acute radiation toxicities such as mucositis, xerostomia and dysphagia. Although acute symptoms subside over time, in the case of patients who have to continue treatment, they may have problems. PPEG may temporarily overcome this problem with bypassing the food into the stomach, thus nutrition is continuously maintained. The nourishment effects diminish migration from 2nd grade to 3rd grade weight loss in that period.

Concerning treatment toxicity, we found that there were no haematological and renal toxicity differences between the PPEG and non-PPEG groups, which were similar to findings of other PPEG studies in other head and neck cancers (Lee et al., 1998; Assenat et al., 2011). However the effect of PPEG on patient's potassium status was different between the groups. Patients with PPEG developed grade 3 hypokalemia less than in the non-PPEG group, which was not mentioned in the other studies.

In this study, PPEG does not influence treatment compliance. Nugent et al. (2010) also reported that the method of enteric feeding did not influence radiotherapy treatment interruptions and Paccagnella et al. (2010) found that early nutritional intervention can reduce patients who develop radiation treatment break more than 5 days, from and total number of days of delayed radiation. These may be interpreted, as only PPEG insertion could not refer to good nutritional care. Normally, patients will try to have liquids or solids via oral route although they have PPEG. The total calorie intake will not be enough to maintain nutritional status with only food taken via the mouth. Therefore, the patient's intake must be evaluated over the course of treatment as a practice.

Duration of PEG dependence was an average of 274 (181-294) days in our study and 148-285 days in systematic review (Paleri and Patterson, 2010). Usually prolonged PEG dependence can lead to poor quality of life. The risk of developing a swallowing dysfunction will increase, if patients don't have per oral within a period of more than 2 weeks. However, some patients did not use PPEG during the course of treatment.

Information from the cross sectional study show 47.8% of PPEG patients never used or used it less than 2 weeks (Madhoun et al., 2011). Although a randomized study that closed early because of poor accrual showed PPEG is not different from a nasogastric tube in maintaining weight during radiation treatment (Corry et al., 2008). Then PPEG is occasionally a needless procedure. Currently, the indication of PPEG in head and neck cancer treatment remains unclear. A national survey in the United Kingdom could not conclude the consensus (Moor et al., 2010). The consideration of PPEG should be used with deliberation.

There were some limitations in this study. The retrospective approach might have a risk of selection bias. The PPEG's insertion in nasopharyngeal carcinoma patients who will undergo chemoradiation is a policy of our institution. However, some patients did not opt for PPEG due to either the doctor's or patient's judgment, or socioeconomic problems. The patient in PPEG

group had better performance status with lower risk of critical weight loss. If this parameter is not different, the contrast of weight loss between groups may be shown more pronounced (Nourissat et al., 2010). Secondly, doctors attempted to give and complete the schedule of chemotherapy; they had to adjust chemotherapy doses or change from cisplatin to carboplatin because of treatment complications. Although changing from cisplatin to carboplatin was not different between the two groups, the dose reduction was not analysed in this study.

In conclusions, PPEG could decrease number of patients who experienced severe weight loss, reduced migration from 2nd grade to 3rd grade weight loss and reduced hypokalaemia. However, the benefits in treatment compliance cannot be detected. So consideration of PPEG in nasopharyngeal carcinoma patients should be used with carefulness.

Acknowledgements

We are grateful to the colleagues in the Therapeutic Radiology and Oncology Unit, Faculty of Medicine, Prince of Songkla University for the convenience of data collection. We are also thankful to Mrs. Jude Hall, Mr. Trevor Pearson and Mr. David Leather from international affair unit for proofreading.

References

Al-Sarraf M, LeBlanc M, Giri PG, et al (1998). Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099. *J Clin Oncol*, **16**, 310-7.

Assenat E, Thezenas S, Flori N, et al (2011). Prophylactic percutaneous endoscopic gastrostomy in patients with advanced head and neck tumors treated by combined chemoradiotherapy. *J Pain Symptom Manage*, **42**, 548-56.

Bahl M, Siu LL, Pond GR, et al (2004). Tolerability of the Intergroup 0099 (INT 0099) regimen in locally advanced nasopharyngeal cancer with a focus on patients' nutritional status. *Int J Radiat Oncol Biol Phys*, **60**, 1127-36.

Capuano G, Grosso A, Gentile PC, et al (2008). Influence of weight loss on outcomes in patients with head and neck cancer undergoing concomitant chemoradiotherapy. *Head Neck*, **30**, 503-8.

Capuano G, Gentile PC, Bianciardi F, et al (2010). Prevalence and influence of malnutrition on quality of life and performance status in patients with locally advanced head and neck cancer before treatment. *Support Care Cancer*, **18**, 433-7.

Chen AM, Li BQ, Lau DH, et al (2010). Evaluating the role of prophylactic gastrostomy tube placement prior to definitive chemoradiotherapy for head and neck cancer. *Int J Radiat Oncol Biol Phys*, **78**, 1026-32.

Chang JH, Gosling T, Larsen J, et al (2009). Prophylactic gastrostomy tubes for patients receiving radical radiotherapy for head and neck cancers: a retrospective review. *J Med Imaging Radiat Oncol*, **53**, 494-9.

Chongsuvivatwong V (2011). epicalc: Epidemiological calculator, version 2.12.2.3 http://CRAN.R-project.org/package=epicalc, Accessed 10 Jun 2012.

Corry J, Poon W, McPhee N, et al (2008). Randomized study of percutaneous endoscopic gastrostomy versus nasogastric tubes for enteral feeding in head and neck cancer patients treated with (chemo)radiation. *J Med Imaging Radiat Oncol*, **52**, 503-10.

Datema FR, Ferrier MB, Baatenburg de Jong RJ (2011). Impact of severe malnutrition on short-term mortality and overall survival in head and neck cancer. *Oral Oncol*, **47**, 910-4.

Gault MH, Longerich LL, Harnett JD, Wesolowski C (1992). Predicting glomerular function from adjusted serum creatinine. *Nephron*, **62**, 249-56.

Lee JH, Machtay M, Unger LD, et al (1998). Prophylactic gastrostomy tubes in patients undergoing intensive irradiation for cancer of the head and neck. *Arch Otolaryngol Head Neck Surg*, **124**, 871-5.

Madhoun MF, Blankenship MM, Blankenship DM, Krempl GA, Tierney WM (2011). Prophylactic PEG placement in head and neck cancer: how many feeding tubes are unused (and unnecessary)? *World J Gastroenterol*, **17**, 1004-8.

Mercuri A, Lim JD, Wada M, Rolfo A, Khoo V (2009). The effect of an intensive nutritional program on daily set-up variations and radiotherapy planning margins of head and neck cancer patients. *J Med Imaging Radiat Oncol*, **53**, 500-5.

Moor JW, Patterson J, Kelly C, Paleri V (2010). 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)*, **22**, 192-8.

Nourissat A, Bairati I, Samson E, et al (2010). Predictors of weight loss during radiotherapy in patients with stage I or II head and neck cancer. *Cancer*, **116**, 2275-83.

Nugent B, Parker MJ, McIntyre IA (2010). Nasogastric tube feeding and percutaneous endoscopic gastrostomy tube feeding in patients with head and neck cancer. *J Hum Nutr Diet*, **23**, 277-84.

Paccagnella A, Morello M, Da Mosto MC, et al (2010). Early nutritional intervention improves treatment tolerance and outcomes in head and neck cancer patients undergoing concurrent chemoradiotherapy. *Support Care Cancer*, **18**, 837-45.

Paleri V, Patterson J (2010). Use of gastrostomy in head and neck cancer: a systematic review to identify areas for future research. *Clinical Otolaryngology*, **35**, 177-89.

R Foundation for Statistical Computing (2008). R: A language and environment for statistical computing. http://www.r-project.org/, Accessed 10 Jun 2012.

Salas S, Baumstarck-Barrau K, Alfonsi M, et al (2009). 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*, **93**, 503-9

Silander E, Nyman J, Bove M, et al (2011). Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer - a randomized study. *Head Neck*, **34**, 1-9.