Clinical Oncology (2005) **17**: 639–645
doi:10.1016/j.clon.2005.03.015

Original Article

Nutrition Support Improves Patient Outcomes, Treatment Tolerance and Admission Characteristics in Oesophageal Cancer

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ABSTRACT:
Aims: Patients with oesophageal cancer undergoing chemoradiation with curative intent are at high risk of malnutrition and its complications, including increased side effects of treatment. We have developed a nutrition pathway (NP), involving the early then periodic nutrition assessment of all patients presenting to the multidisciplinary oesophageal clinic who were planned to receive definitive chemoradiation.
Materials and methods: Patients were assessed as at 'low', 'moderate' or 'severe' nutrition risk, and were provided with appropriate nutrition intervention ranging from preventative advice (low risk), oral nutrition support (moderate risk) to enteral feeding (severe risk). Outcomes for 24 patients treated before implementation of the NP were compared with those of 24 patients treated using the NP.
Results: Patients managed using the NP experienced less weight loss (mean weight change -4.2 kg ± 6.4 cf. -8.9 kg ± 5.9, $P = 0.03$), greater radiotherapy completion rates (92% cf. 50%, $P = 0.001$), fewer patients had an unplanned hospital admission (46% cf. 75%, $P = 0.04$), and those that did had a shorter length of stay (3.2 days ± 5.4 cf. 13.5 days ± 14.1, $P = 0.002$).
Conclusion: Early and regular nutrition assessment/intervention and a multidisciplinary approach to nutrition care results in improved treatment tolerance for patients with oesophageal cancer receiving chemoradiation. Odelli, C. *et al*. (2005). *Clinical Oncology* **17,** 639–645

Key words: Cancer, enteral nutrition, nutrition support, oesophageal cancer

Received: 30 July 2004 Revised: 17 February 2005 Accepted: 8 March 2005

Introduction

Patients with cancer of the oesophagus are often malnourished at presentation [1,2]. Dysphagia has been found to be the primary symptom in more than 90% of patients [3], and this has an adverse effect on nutritional status.

Treatments for oesophageal cancer are commonly multimodal, incorporating polychemotherapy, radiotherapy and surgery [4,5]. These treatments frequently cause or exacerbate poor nutritional status through commonly experienced side effects, such as nausea, vomiting, anorexia, lethargy, diarrhoea, oesophagitis and dysphagia [6,7]. Malnutrition has been found to negatively affect response to therapy and survival in oncology patients [8,9]. It increases the length of hospital stays [8] and is associated with higher health-care costs, slower healing, increased complications and higher mortality rates [10,11].

Over recent years, a growing body of literature has examined the role of aggressive nutrition support, through percutaneous endoscopic gastrostomies (PEGs), aimed at correcting or preventing malnutrition during treatment for head and neck, and oesophageal malignancies.

Studies have shown that PEGs are a feasible, safe method of delivering nutrition support to this group of patients [12–18]. Some studies have focused on identifying indicators to target those patients who require this type of aggressive nutrition support [14,19]. Other studies demonstrate nutritional status and rate of hospitalisation benefits when patients are supported in this manner [14–16,20–22]. Margolis *et al.* [15] showed PEG placement before treatment to be significantly related to attainment of target doses of chemoradiation and survival at 1 year.

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0936-6555/05/000000+07 $35.00/0

The Newcastle Mater Misericordiae Hospital (NMMH) is the tertiary referral centre for oncology patients in the Hunter New England Area Health Service. Before 1996, the nutrition management of patients receiving definitive chemoradiation for oesophageal cancer was reactive and often occurred late in the treatment period. Debilitating weight loss and frequent unplanned hospital admissions were a significant management problem.

In 1996, a newly formed multidisciplinary oesophageal clinic, comprising medical and radiation oncologists, a thoracic surgeon and a dietitian, devised a nutrition pathway (NP) to improve the nutritional management of patients with oesophageal cancer. The NP was developed by the investigators on the basis of their clinical experience and a literature review [8,9,11,23–25]. Levy *et al.* [24] made a number of recommendations based on the work of Shils [26] on nutritional support for oncology patients, including (1) a therapeutic diet plan that analyses factors contributing to nutrition depletion; (2) early and periodic assessment of nutritional status; (3) nutrition support, initiated early when indicated; (4) optimal nutrition care requires a multidisciplinary approach.

More recently, these recommendations have been incorporated into Medical Nutrition Therapy Protocols [27]. The NP also incorporated these recommendations into a specific pathway designed to facilitate the challenging nutritional management of patients with oesophageal cancer receiving definitive chemoradiation (Fig. 1).

The NP promoted a proactive approach to nutrition intervention, ensuring that early and aggressive dietetic intervention occurred. The NP also provided management guidelines for the initiation and maintenance of nutrition support throughout the treatment course. We report here a retrospective evaluation of the NP. The outcomes studied were weight status, percentage of planned treatment delivered, number of unplanned hospital admissions (UHA) and length of hospital stay during treatment.

Methods

Eligible patients were planned to receive definitive, synchronous chemoradiation for oesophageal cancer over the study period (1990–2001). Most patients were entered on the Trans Radiation Oncology Group (TROG) trials 89-04, 96-02 or 98-06. Previously untreated patients were planned to receive the chemotherapy regimen cisplatin 80 mg/m^2 by IV infusion on day 1 and day 21 (or day 28) plus 5-fluorouracil 800 mg/m^2 by continuous infusion on days 2–5 and days 22–25 (or days 29–32). Patients were planned to receive radiation to a dose of 60 Gy to the tumour-bearing volume and 30 Gy to the regional lymphatics using daily incremental fractions of 2 Gy over 6 weeks.

A retrospective chart review was undertaken in 2002. The review compared outcomes for two groups of patients: historical control group ($n = 24$), which consisted of any patient planned to receive this definitive treatment for oesophageal cancer from 1990 to 1996 (i.e. before NP); and the NP group ($n = 24$), which consisted of any patient presenting to the oesophageal clinic from 1997 to 2001 who was planned for definitive treatment as described above. These patients were managed according to the NP protocol.

The control group had received nutrition support in a reactive manner. Patients were referred to dietitians only as problems arose, and this meant that initiation of appropriate nutrition support commenced later in the treatment protocol. The control group was classified retrospectively as at low/moderate/severe nutrition risk at presentation according to the predetermined assessment criteria defined by the NP (Fig. 1). The NP group was automatically interviewed by the dietitian at initial presentation to the oesophageal clinic. Patients in the NP group were classified at presentation as at low/moderate or severe nutrition risk according to the NP assessment criteria (Fig. 1). According to the NP protocol, patients in the NP group identified as at 'low' risk received information and support to help maintain nutritional status, whereas those at 'moderate' risk received consistency modified, high protein/high energy diet education. All patients were reviewed weekly throughout the treatment course as per the NP protocol. Patients who crossed over from 'low/moderate' risk to 'severe' risk during the course of treatment had PEG or nasogastric tube placement, depending on the treatment week in which this occurred. PEGs were organised for severe risk patients ($n = 10$) before starting treatment in all cases, and instruction for home use was provided.

Patients in both groups requiring enteral nutrition were managed in the same manner. The enteral feed chosen was a 1.5 kcal/ml feed, nutritionally complete in 1690 kcals. Regular follow-up of all patients receiving enteral nutrition took place to assess nutritional status, and nutrient prescriptions were adjusted if necessary.

Data that included the timing and type of dietetic intervention, weight change over treatment course, percentage of planned treatment delivered, treatment breaks and delays, UHAs and length of stay for UHAs was retrieved for the two groups of patients. The study was limited to the period during which the treatment took place.

Results were analysed using the statistics package SPSS 10.0 for Windows (SPSS Inc, Chicago, Illinois). Categorical variables were analysed by chi-squared or Fisher's Exact test as appropriate. Differences in continuous variables between groups were compared using Students *t*-test or Mann–Whitney test, depending on distribution. All statistical analyses were two-tailed and a value of $P < 0.05$ was considered statistically significant.

Results

The control group was well matched with the NP group for age, tumour position/length, weight loss and dysphagia at initial presentation to the oesophageal cancer clinic (Table 1). The number of patients in each nutrition risk category was similar for the two groups.

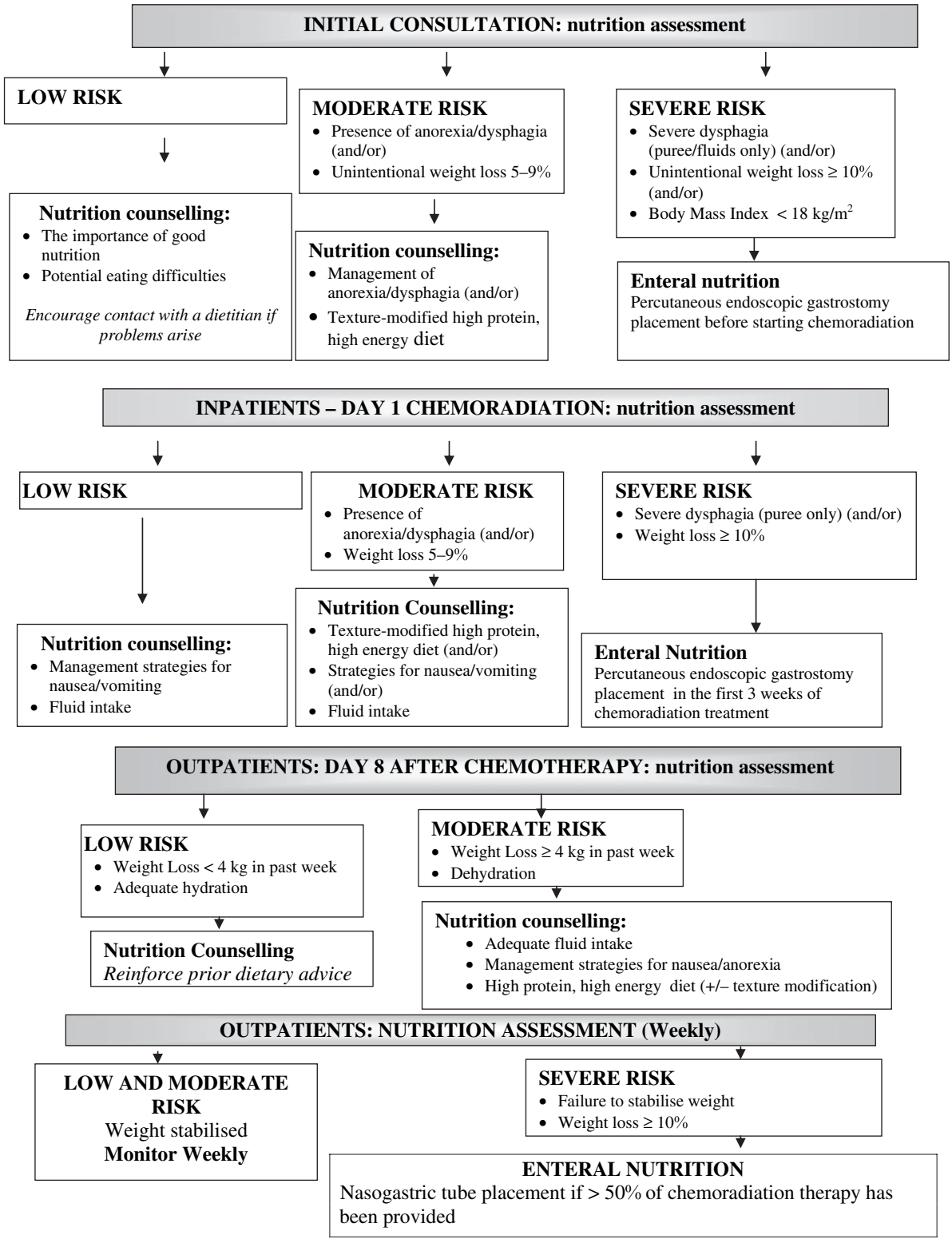

Fig. 1 – Nutritional management of patients with oesophageal cancer receiving definitive chemoradiation.

Table 1 – Comparison of demographic, oncological and nutritional characteristics of 48 control and nutrition pathway patients receiving definitive chemoradiation for oesophageal cancer

	Control ($n = 24$)	NP ($n = 24$)	P value
Sex, male (%)	67	71	0.77
Age (years)*	71.9 (±9.8)	66.4 (±10.9)	0.07
Tumour type (%)			
Squamous cell	71	71	
Adenocarcinoma	29	29	1.00
Tumour length (cm)*	6.1 (±2.2)	6.3 (±3.2)	0.34
Tumour position (%)			
Top	17	8	0.79
Middle	17	26	
Lower	58	58	
Oesophago-gastric junction	8	8	
Patients with dysphagia (%)	92	83	0.38
Usual body mass index* (kg/m^2)	25.5 (±5.1)	27.4 (±6.1)	0.27
Weight loss at presentation compared with usual weight (%)*	7.3 (±5.6)	7.4 (±6.3)	0.92
Nutrition risk (%)			
At low risk	21 ($n = 5$)	16 ($n = 4$)	0.47
At moderate risk	25 ($n = 6$)	42 ($n = 10$)	
At severe risk	54 ($n = 13$)	42 ($n = 10$)	

*Expressed as mean (±standard deviation) for normal variables. NP, nutrition pathway.

Table 2 – Comparison of timing and reasons for initial dietetic intervention for 48 patients in the control and nutrition pathway groups receiving definitive chemoradiation for oesophageal cancer

	Control ($n = 24$)	NP ($n = 24$)	P value
Patients (%) with first intervention at			
First presentation to unit	38 (9)	96 (23)	<0.05
Start of treatment	29 (7)	4 (1)	
During treatment*	33 (8)	0 (0)	
Reason for intervention (%)			
Dysphagia	100 (24)	83 (20)	0.04
Weight loss	83 (20)	79 (19)	>0.05
Anorexia	46 (11)	46 (11)	>0.05
Automatically referred because of NP operation	0 (0)	96 (23)	<0.05
Referred for other reasons†	21 (5)	17 (4)	>0.05

*Intervention occurred week 2 ($n = 6$), week 3 ($n = 1$), week 7 ($n = 1$). †Other reasons for referral in control group: enteral nutrition required pre-treatment ($n = 2$); low albumin/diabetes/nausea ($n = 1$ patient each). Other reasons for referral in NP group: enteral nutrition review as enteral nutrition had been commenced elsewhere ($n = 1$); reflux/social situation/diabetes ($n = 1$ patient each). NP, nutrition pathway.

There were, however, significant differences between the groups in timing and indication for dietetic interventions that reflected the operation of the Pathway (Table 2).

Automatic referral as a reason for intervention at presentation occurred in 23 out of 24 patients in the NP group, highlighting excellent compliance (96%) with the protocol. In the control group, 33% of patients were not seen by a dietitian until at least the second week of treatment, with one patient not referred until week 7 of treatment. Table 3 compares enteral nutrition (EN) delivered to both groups. Thirteen patients in the control group (13/24, 54%) were assessed retrospectively as 'severe nutrition risk', but only in two cases was pre-treatment nutrition support through a PEG initiated. In contrast, the 10 NP patients (10/24, 42%) assessed as at severe risk all received a PEG pre-treatment.

There was a significant difference in the timing of EN intervention between the groups; however, the total number of patients receiving EN was not different (Table 3). Patients in the NP group lost less weight over the treatment period (Table 4).

The NP had no effect on chemotherapy delivery compared with controls. There was a trend towards fewer dose reductions in patients in the NP group (Table 5). However, a striking difference was observed in the percentage of patients who completed the planned radiotherapy course: 92% of the NP group compared with 50% of the control group, $P = 0.003$ (Table 6). The percentage dose of radiotherapy delivered to the NP group (median 100, 50–100) was also more than the percentage dose delivered to the control group (median 95, 35–100) ($P = 0.004$). In the control group, nine out of 12 patients discontinuing treatment did so because of side effects, whereas only two patients in the NP group did not complete treatment, and both because of coincidental myocardial infarctions.

Patients in the control group were more likely to have a UHA during the treatment period (Table 7), with 75% of control patients having a UHA compared with 46% of patients in the NP group ($P = 0.04$). Although the total number of UHA was not different between the groups ($P = 0.05$), the total length of stay for all UHA was greatly reduced in the NP group: 13.5 days (±14.1) for the control group compared with 3.2 days (±5.4) for the NP group ($P = 0.002$) (Table 7). Only one patient in the NP group was admitted for enteral nutrition (1/11, a 1-day admission for PEG placement for a patient crossing over from moderate to severe risk), whereas six of the 18 admissions in the control group patients were primarily for nutritional support.

Discussion

This study shows that nutrition intervention delivered according to the NP had a significant positive affect on

Table 3 – Comparison of enteral nutrition delivered to patients in the control and nutrition pathway groups receiving definitive chemoradiation for oesophageal cancer

	Control ($n = 8$)	NP ($n = 13$)	P value
Patients receiving enteral nutrition (%)	33 (8/24)	54 (13/24)	>0.05
Enteral nutrition started (week)	3.6 (±3.0)	−0.31 (±2.8)	0.001
Administration method (%)			
PEG	25 (2)	77 (10)	0.06
Nasogastric	63 (5)	15 (2)	
Nasogastric then PEG	12 (1)	8 (1)	
Body Mass Index at start of enteral nutrition (kg/m^2)*	19.0 (±3.6)	22.3 (±4.1)	0.08
Usual weight lost at start of enteral nutrition (%)*	17.9 (±5.5)	12.3 (±4.7)	0.02
Problems during enteral nutrition (%)			
Nausea	38 (3)	46 (6)	>0.05
Diarrhoea	13 (1)	0 (0)	>0.05
Bloating	38 (3)	46 (6)	>0.05
Tube blockage	13 (1)	23 (3)	>0.05
Vomiting	25 (2)	15 (2)	>0.05
Tube dislodgement	13 (1)	0 (0)	>0.05
Reflux	13 (1)	15 (2)	>0.05
PEG site infection	0(0)	8(1)	>0.05
Patients receiving enteral nutrition by nutrition risk assessment (%)			
Severe risk	38 (5/13)	100 (10/10)	0.003
Moderate risk	33 (2/6)	30 (3/10)	>0.05
Low risk	20 (1/5)	0 (0/10)	>0.05

*Expressed as mean (±standard deviation) for normal variables. NP, nutrition pathway; PEG, percutaneous endoscopic gastrostromy.

nutritional status and treatment tolerance during definitive chemoradiation for oesophageal cancer.

Patients in the NP group lost less weight throughout the treatment period, were less likely to have a UHA and had a shorter hospital stay if they did have a UHA. The NP group also received significantly more of the planned radiotherapy dose.

Aggressive nutrition support, often involving the prophylactic placement of PEGs before treatment in patients receiving treatment for head and neck, and oesophageal

Table 4 – Comparison of weight outcomes for 48 patients in the control and nutrition pathway groups receiving definitive chemoradiation for oesophageal cancer

	Control ($n = 16$) completed	NP ($n = 22$) completed	P value
Usual weight lost at end of treatment (%)*	16.2 (±6.8)	11.0 (±4.9)	0.04
Weight change during treatment (%)*	−8.9 (±5.9)	−4.2 (±6.4)	0.03
Weight change over treatment course/nutrition risk (%)*			
Severe	−6.33 (±6.0)	0.38 (±6.1)	0.06
Moderate	−11.8 (±7.6)	−8.0 (±6.3)	0.48
Low	−9.5 (±4.4)	−6.3 (±4.9)	0.21

*Values expressed as mean ± standard deviation for normal variables.

Table 5 – Comparison of chemotherapy outcomes for 48 patients in the control and nutrition pathway groups receiving definitive chemoradiation for oesophageal cancer

	Control ($n = 24$)	NP ($n = 24$)	P value
Treatment received			
Two cycles of cisplatin and 5-FU	92 (22)	83 (20)*	0.33
One cycle of cisplatin and 5-FU	8 (2)	4 (1)	
One cycle of cisplatin and two cycles of 5-FU	0 (0)	8 (2)	
Half cycle of cisplatin and 5-FU	0 (0)	4 (1)	
Patients experiencing chemotherapy delay (%)	71 (17)	67 (16)	
Number of weeks delay†	Median 1 (0–3)	Median 1 (0–3)	0.40
Patients who had a dose reduction (%)	42 (10)	29 (7)	0.34
Planned cisplatin dose received (%)†	Median 100 (50–100)	Median 100 (50–100)	0.40
Planned 5-FU dose received (%)†	Median 100 (50–100)	Median 100 (50–100)	0.29

*Three patients in group 2 had four cycles of cisplatin/5-FU, but only the first two cycles were included in the analysis.
†Median (range) reported for non-normal variables. 5-FU, 5-fluorouracil; NP, nutrition pathway.

Table 6 – Comparison of radiotherapy outcomes for 48 patients in the control and nutrition pathway groups receiving definitive chemoradiation for oesophageal cancer

	Control ($n = 24$)	NP ($n = 24$)	P value
Patients who completed radiotherapy (%)	50 (12)	92 (22)	0.001
Patients who had radiotherapy break (for those who completed treatment) (%)	33 (4/12)	27 (6/22)	0.71
Number of days break (for those who completed treatment)*	0 (0–18)	0 (0–13)	0.48
Planned radiotherapy dose delivered (%)*	Median 95 (37–100)	Median 100 (60–100)	0.004
Radiotherapy dose delivered/nutrition risk (%)*			
Severe	83 (37–100)	100 (60–100)	0.06
Moderate	100 (58–100)	100 (93–100)	0.20
Low	100 (50–100)	100 (100–100)	0.18

*Values expressed as median (+ range) for non-normal variables. NP, nutrition pathway.

Table 7 – Comparison of hospital admissions outcomes for 48 patients in the control and nutrition pathway groups receiving definitive chemoradiation for oesophageal cancer

	Control ($n = 24$)	NP ($n = 24$)	P value
Patients who had a UHA (%)	75 (18)	46 (11)	0.04
Number of UHA per patient*	Median 1 (0–2)	Median 0 (0–4)	0.05
Total number UHA per group	24	16	
Total length of stay for all UHA (days)†	13.5 (±14.1)	3.2 (±5.4)	0.002
Length of stay admission 1 (days)*	Median 6.5 (0–52)	Median 0 (0–11)	0.002
Length of stay admission 2 (days)*	Median 0 (0–31)	Median 0 (0–17)	>0.05
Reason for admission 1: for enteral nutrition (%)	33 (6/18)	9 (1/11)	>0.05
Reason for admission 2: for enteral nutrition (%)	17 (1/6)	0 (0/3)	>0.05
Total length of stay/ nutrition risk (days)†			
Severe	16 (0–52)	2 (0–8)	0.006
Moderate	2.5 (0–11)	0 (0–20)	>0.05
Low	16 (0–34)	2 (0–16)	>0.05

*Values expressed as median (range) for non-normal variables.
†Values expressed as mean (±standard deviation) for normal variables.
UHA, unplanned hospital admission. NP, nutrition pathway.

malignancies, has repeatedly shown nutritional status and rates of hospitalisation benefits [12,14,16,20].

UHAs and length of stay for these UHAs have financial implications for the health system. Nutrition support using the NP was delivered on an out-patient basis. The cost of an oncology bed in April 2002 was $360/day. In contrast, the cost of nutritionally supporting patients at home using enteral nutrition was about $8.50 per day (April, 2002). Patients in the control group had a mean total length of stay of 13.5 days (±14.1), whereas those in NP group had a mean total length of stay of 3.2 days (±5.4) (Table 6), so the overall cost saving to the health system of proactive nutritional support delivered in this way is substantial.

A clinically important finding was that the NP facilitated the delivery of the planned radiotherapy treatment. Patients in the NP group were more likely to complete the radiotherapy course, and received more of the planned radiotherapy dose, although no affect on chemotherapy dose delivered was found. Margolis *et al.* [15] routinely placed PEGs before treatment with chemoradiation in a similar group of oesophageal cancer patients, and found PEG use to be significantly related to attainment of target doses of chemoradiotherapy and also survival at 12 months. Bozzetti *et al.* [21] found they could deliver the same dose of pre-surgery chemoradiation to both high- and low-risk oesophageal cancer patients if they nutritionally supported the high-risk group with EN with a nasogastric tube throughout the treatment course. However, no survival difference was noticed. The main determinant of the outcome of cancer treatment is the efficacy of the cancer therapy; however, studies have found that radiotherapy treatment breaks and delays can affect locoregional control and survival [28,29]. Therefore, nutrition support that facilitates the delivery of planned treatment may ultimately confer survival benefits. Owing to the retrospective nature of this study, and the lack of a complete set of follow-up data, survival was not an outcome assessed.

Proactive nutrition support was a key feature of the NP. A number of recent studies have emphasised the need for a proactive approach to nutrition in patients with head and neck or oesophageal malignancies who are to undergo treatments known to cause significant nutritional compromise [13–15,17,21]. In the environment of a multidisciplinary clinic, the NP and proactive nutrition support were easy to adopt and were readily accepted by the patient, as all members of the team repeatedly reinforced to patients the role of nutrition in the treatment course.

When devising the NP, the investigators considered the question: 'do all oesophageal cancer patients planned for definitive chemoradiation require PEG placement before treatment?' Clinical experience showed that some patients did tolerate the challenging treatment without significant affect on nutritional status. Dysphagia at presentation, limiting intake to puree consistency or weight loss 10% or more of usual body weight and/or body mass index of 18 or less were identified as indicators highlighting severe nutrition risk necessitating pre-treatment PEG placement. In contrast, Stockel *et al.* [13] and Margolis *et al.* [15] used PEGs routinely in all oesophageal cancer patients presenting for chemoradiation, whereas Bozzetti *et al.* [21], in their cohort of oesophageal cancer patients, used dysphagia as the criteria for feeding. Piquet *et al.* [14] applied indicators of weight loss more than 10% or body mass index less than 20, or age over 70 years to identify patients for pre-treatment PEGs in a group of patients with oropharyngeal cancer planned for radiotherapy. The assessment indicators used in the NP adequately discriminated levels of nutritional risk. For patients classified as at moderate nutritional risk, 33% of control patients and 30% of NP patients required enteral nutrition to be initiated during the course of treatment. Only one patient classified as low nutrition risk went on to receive enteral nutrition.

This study has limitations because it was a retrospective chart audit. Although case matching was not possible, no differences were found between the control group and the NP group in variables that could be expected to affect outcomes (Table 2). There were also, in effect, no differences in treatment protocols for the two groups. Given the recognition of the effects of malnutrition and the potential benefits of nutrition support, it would have been unethical to withhold nutrition support from this vulnerable group.

Conclusion

Implementation of this NP has been associated with improved clinical outcomes, including decreased weight loss, number of UHAs and length of stay during the

treatment course, and a higher tolerance of planned treatment. We recommend that all patients with oesophageal cancer planned for definitive chemoradiation receive a proactive nutritional assessment by a specialist oncology dietitian on initial presentation, and appropriate nutritional support and follow-up within the multidisciplinary team.

Acknowledgements. L. Francis and B. Aldrich (Department of Radiation Oncology, NMMH) for assistance with the Statistics Package, SPSS 10.0; J. Kilmurray (Department of Radiation Oncology, NMMH) for technical assistance; F. McLean (Department of Dietetics, Gosford Hospital) for assistance with the manuscript; M. Diamantes for assistance with the manuscript. This research was supported by a Margaret Mitchell Research Grant.

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