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ORIGINAL ARTICLE

Validation of an updated evidence-based protocol for proactive gastrostomy tube insertion in patients with head and neck cancer

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BACKGROUND/OBJECTIVES: Evidence-based practice guidelines are available to assist in the decision making for nutrition interventions in patients with head and neck cancer. Re-assessment of guideline recommendations is important with changing demographics, new treatment regimens, advancing radiotherapy techniques, such as helical intensity-modulated radiotherapy, and the emergence of new literature. The aim of this study was to validate the updated high-risk category definition in our local hospital protocol for the swallowing and nutrition management of patients with head and neck cancer to determine the ongoing predictive ability for identifying proactive gastrostomy requirement in a new cohort.

SUBJECTS/METHODS: Patients attending a major tertiary hospital for head and neck cancer treatment from 2010 to 2011 were included ($n = 270$). Data were collected on patient demographics (age and gender), clinical factors (tumour site, staging and treatment), nutrition outcome measures (weight, enteral feeding) and protocol adherence. Sensitivity and specificity were calculated and compared with the original validation study.

RESULTS: Proactive gastrostomy tubes were inserted in 86 patients. Overall protocol adherence was 93%. Sensitivity improved to 72% (increase of 18%) and specificity improved to 96% (increase of 3%) compared with the original validation study where patients received three-dimensional (3-D) conformal radiotherapy.

CONCLUSIONS: The results of this study confirm that the updated high-risk category in the protocol for the swallowing and nutrition management of patients with head and neck cancer remains valid to predict proactive gastrostomy in a mixed population receiving helical intensity-modulated radiotherapy and 3-D conformal radiotherapy. The protocol has an improved sensitivity and specificity and hence remains just as relevant for advanced techniques of radiation treatment delivery.

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INTRODUCTION

Patients with squamous cell carcinoma of the head and neck frequently experience dysphagia as a result of cancer treatment or the tumour itself, which often results in a need for tube feeding to provide adequate nutritional intake. The optimal form of tube feeding remains controversial in the literature, with inadequate high-level evidence to enable any firm recommendations.[1–3] Risks of gastrostomy placement in the selection of feeding tube need to be considered.[4] Some studies have shown benefits with prophylactic gastrostomy placement compared with a reactive approach to nutrition support including reduced weight loss/improved nutritional status,[5–8] improved quality of life[9] and reduced admissions and health-care costs.[10,11] Other studies have shown no difference in outcomes with feeding tube selection and suggest that a reactive approach may be more favourable to reduce duration of feeding tube use.[12,13] Although there are concerns that gastrostomy placement may result in gastrostomy dependency and increased dysphagia post treatment,[14,15] other studies have not supported this finding.[16,17]

A hospital protocol for the swallowing and nutrition management of patients with head and neck cancer was developed at our institution in order to help clinicians identify high-risk patient groups who would benefit from proactive gastrostomy placement. The risk categories in the protocol have been validated for their ability to predict the need for proactive gastrostomy placement in a patient population receiving three-dimensional (3-D) conformal radiotherapy.[18] Implementation of the protocol has been shown to reduce unplanned hospital admissions and length of stay,[10] and adherence to the protocol has been demonstrated to improve nutrition outcomes.[19] The protocol was subsequently modified following availability of new evidence[20] and further internal evaluation to improve their accuracy and validity,[21] which resulted in some changes to the high-risk category definition (Figure 1 and Supplementary Appendix 1).

Evolving radiotherapy techniques, such as conformal radiotherapy or linear accelerator-based intensity-modulated radiation therapy (IMRT), have been used in recent years with the aim of limiting the radiation dose to healthy tissues and organs to minimise unwanted side-effects. Around the same time of implementation of the updated protocol, a new radiotherapy technique Helical-IMRT (H-IMRT) was also introduced at our hospital. This is a relatively new type of IMRT delivery system using a Tomotherapy machine. It further limits radiation damage to normal tissue compared with IMRT and thereby results in less

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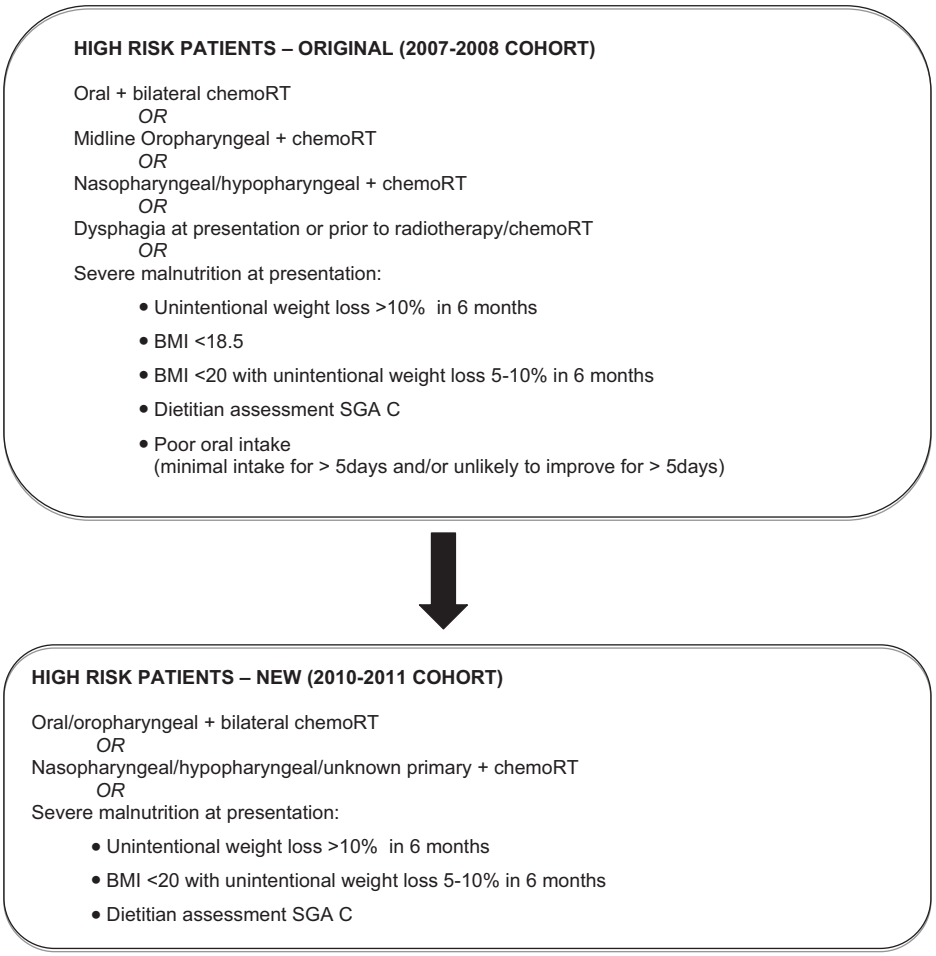

Figure 1. Comparison of the high-risk category of the Royal Brisbane and Women's Hospital Protocol for the swallowing and nutrition management of patients with head and neck cancer for each cohort. Abbreviations: chemoRT, chemoradiotherapy; BMI, body mass index; SGA, subjective global assessment. Adapted from Brown *et al.*[18] (Copyright © 2012 Wiley Periodicals, Inc.)

long-term side-effects of radiation.[22,23] To date the majority of studies investigating nutrition outcomes and tube-feeding requirements have been undertaken in patients receiving 3-D conformal radiotherapy or IMRT, and therefore the nutritional needs of patients following H-IMRT are largely unknown.

In addition, in recent years, there has been an increasing incidence of human papillomavirus (HPV)-related head and neck tumours.[24] These patients present with distinct carcinogenesis, risk factors, clinical presentation and prognosis compared with HPV-negative patients,[25–30] resulting in a change of clinical and demographical profile of the population. Patients with HPV-positive tumours show better response to treatment, overall survival and progression-free survival,[25] and therefore research into alternative treatment protocols to reduce toxicities without compromising oncological outcomes is underway.[31]

As treatment methods evolve through technology and further research to optimise patient outcomes, it is important to continue to re-evaluate the evidence for supportive cares such as the nutrition management of this patient population. Therefore, the main aim of this study was to validate the updated high-risk category definition in the protocol for the swallowing and nutrition management of patients with head and neck cancer to determine the ongoing predictive ability for identifying proactive gastrostomy requirement in a new cohort to account for any changes in treatment and population characteristics that are likely to have occurred over the recent years. The second aim was to determine whether there was any impact, specifically from the use of H-IMRT treatment on the applicability of the protocol.

SUBJECTS AND METHODS

Study setting

This is a single institution study where all patients with head and neck cancer attend a multidisciplinary clinic at a tertiary hospital for diagnosis, staging and planning of treatment. All patients are assessed by surgical and medical specialists (ear, nose and throat surgeons; plastic and reconstructive surgeons; oral and maxillofacial surgeons; radiation oncologists and medical oncologists), a dentist, speech pathologist, dietitian and nursing staff. The protocol for the swallowing and nutrition management of patients with head and neck cancer is applied to each patient to assist in the planning of their nutrition management as part of their treatment.

Study population

Patients were eligible for the study if they attended our hospital for assessment and treatment between July 2010 and June 2011. Inclusion criterion was a referral to a dietitian at our hospital, which occurs as part of standard care during curative intent surgical and/or oncological treatment for head and neck cancer. Patients were therefore ineligible if they had the following: benign disease; a non-head and neck tumour; treatment of palliative intent; treatment privately or at another facility or on the short

stay surgical unit. Patients were excluded if there was incomplete data (that is, weight was not recorded or the patient did not complete treatment) or no access to the medical chart (that is, patients did not consent for chart to be used for audit/research purposes or the medical chart was destroyed) The study was deemed a quality-improvement study and exempt from full ethical review by the Human Research Ethical Committee at the Hospital.

Study design and data collection

Data collection was via retrospective chart audit and the use of existing clinical databases. Independent variables included gender, age, clinical factors (tumour site, tumour stage and treatment location), patient risk rating from the protocol (high or low) and adherence to the protocol risk category recommendations. Dependent variables included nutrition outcome measures (percentage weight loss from baseline at diagnosis to the end of cancer treatment), incidence of proactive tube placement and use of this tube, and the incidence of reactive tube placement, including the type of tube and duration of use. Use of the tube was recorded by the dietitian in the medial notes as part of standard assessment on each review during and after treatment. Data on gastrostomy complications rates were also collected for the 30-day period post insertion. Major complications were defined as those requiring surgical intervention, blood transfusion or IV antibiotics. Admissions or prolonged admissions relating to gastrostomy complications were noted.

Outcomes

The dependent variables were used to assess the primary outcome of whether each patient was deemed to require or not require a proactive gastrostomy. Patients were confirmed as high risk, and therefore requiring a proactive gastrostomy, if significant weight loss (⩾10% baseline body weight) had occurred by the end of the acute-phase cancer treatment, or a proactive tube was placed and used or a reactive tube was placed and used for >4 weeks. These outcome definitions are described fully elsewhere[18] and were previously used to confirm the need for intensive early nutrition support intervention, and thus placement of a proactive gastrostomy. A contingency table was used to compare these patient outcomes with the protocol risk category and determine sensitivity, specificity, positive predictive value and negative predictive value. The results were compared with data from the original validation study.

Statistical analysis

Statistical analysis was performed between the current cohort and the historical cohort (used to previously validate the protocol) to determine whether there were any differences between the cohorts' categorical variables and continuous variables, using the χ^2-test and the Independent Samples *t*-test, respectively. Categories were collapsed to enable statistical comparison as follows: Treatment Site (oropharynx and nasopharynx), T Classification (T0 and Tx; recurrent and other), N Classification (other and unknown) and Treatment Type (radiotherapy alone and chemotherapy alone). Age was a continuous variable (years) and presented as mean ± s.d. Levene's test was applied to check assumption of equal population variance prior to the Independent Samples *t*-test. Statistical significance was set at $P < 0.05$. Data were analysed using R Commander Version 1.8–3 and R version 2.14.2 (29 February 2012).

RESULTS

Patient characteristics

There were 551 patients who attended the hospital for assessment during the 1-year study period. After inclusion and exclusion criteria were applied, this gave a final sample size of $n = 270$ for analysis (Figure 2). Patients had a median age of 63 years (range 15–90 years) and were mainly men (77%). The most frequent squamous cell carcinoma of the head and neck sub sites were oral cavity (30%) and oropharynx (24%). Tumour classification was distributed evenly, and 14% of patients presented with recurrent disease. Seventy-five percent of all patients received multimodality treatment. There were 75 patients who received H-IMRT, accounting for 33% of all patients receiving radiotherapy ($n = 230$), with the remainder receiving 3-D conformal radiotherapy. The patient demographics and clinical characteristics are summarised

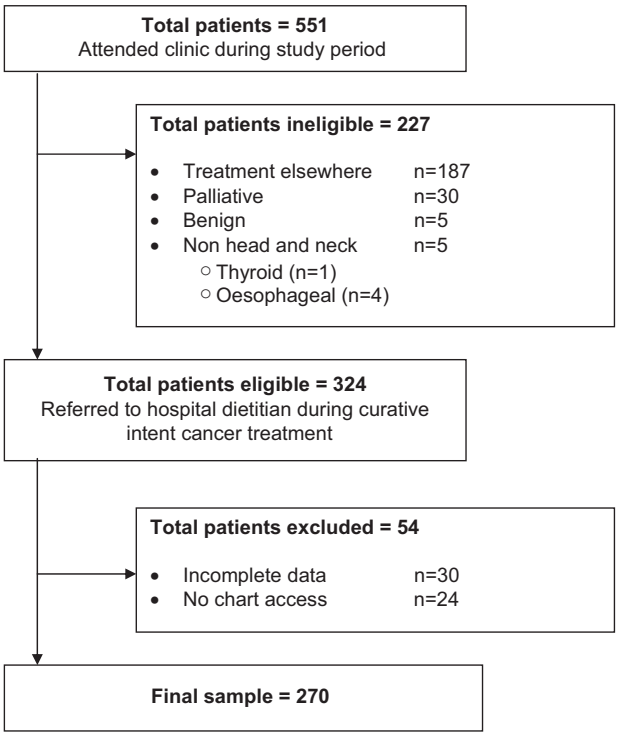

Figure 2. CONSORT diagram to illustrate eligible patient sample with inclusion and exclusion criteria.

in Table 1 and compared with the cohort from the original validation study ($n = 501$). There were no significant differences between the two cohorts with respect to gender or age; however, there were a number of statistically significant differences with respect to tumour site, staging and treatment. In the current cohort, there were a lower proportion of patients with laryngeal cancer, fewer patients with recurrent disease, more patients with N2 disease and fewer patients who received radiotherapy alone (Table 1).

Assessment using the protocol identified 88 patients as high risk, accounting for 33% of the cohort. Reasons for high-risk rating are shown in Figure 3. Of those presenting with severe malnutrition, one patient had radiotherapy for laryngeal cancer, another had radiotherapy for oral cavity cancer and the third had salvage surgery for recurrent disease.

Overall, a gastrostomy tube or nasogastric tube was inserted in 37% ($n = 100$) of patients at some stage during cancer treatment (Table 2). This was very similar to the cohort from the original validation study where it was required in 34% of patients ($n = 173$), ($P = 0.488$).

Gastrostomy complications

Gastrostomy data complications were available for 79/92 patients (12 patients had their tubes placed privately, and 1 patient had an existing tube *in situ*). The rate of major complications from gastrostomy insertion was 3.8% ($n = 3$); one patient required surgical intervention for a laparoscopy and bowel drain; one patient required IV antibiotics for suspected bowel perforation; one patient developed an ileus. An additional three patients had a prolonged admission post insertion managed conservatively, and a further six patients required an admission for IV antibiotics for a site infection.

Adherence to the protocol

Overall adherence with the protocol risk category recommendations by the treating medical team was high (93% compared with

Table 1. Comparison of patient demographics and clinical characteristics from the two cohorts

Patient Characteristics	*Previous 2-year cohort (2007–2008)*		*New 1-year cohort (2010–2011)*		P-*value*
	No. of patients (total n = *501)*	*Frequency (%)*	*No. of patients (total* n = *270)*	*Frequency (%)*	
Age, years (mean ± s.d.)	63.51 ± 12.40		63.15 ± 12.91		P = 0.708
Gender					*P = 0.948*
Male	387	77%	208	77%	
Female	114	23%	62	23%	
Site[a]					*P = 0.004*
Oral cavity	139	28%	81	30%	
Oropharynx	101	20%	65	24%	
Nasopharynx	5	1%	4	2%	
Hypopharynx	16	3%	14	5%	
Larynx	78	16%	18	7%	
Unknown primary	28	6%	9	3%	
Other	134	27%	79	29%	
T classification[b]					*P = 0.080*
T0	0	0%	13	5%	
T1	93	19%	45	17%	
T2	102	20%	69	26%	
T3	71	14%	34	13%	
T4	87	17%	60	22%	
Tx	37	7%	9	3%	
Recurrent	110	22%	38	14%	
Other	1	0%	2	1%	
N classification[c]					*P < 0.001*
N0	176	35%	93	34%	
N1	79	16%	45	17%	
N2	100	20%	88	33%	
N3	14	3%	4	1%	
Recurrent	110	22%	38	14%	
Other	1	0%	2	1%	
Unknown	21	4%	0	0%	
Treatment[d]					*P = 0.023*
Surgery	73	15%	40	15%	
Radiotherapy	85	17%	28	10%	
ChemoRT	143	29%	91	34%	
Surgery+RT	153	31%	96	36%	
Surgery and chemoRT	46	9%	15	6%	
Chemotherapy	1	0%	0	0%	
Additional treatment details					
Tomotherapy	0	0%	75	28%	P < 0.001
Cetuximab	34	7%	16	6%	P = 0.538

Abbreviation: RT, radiotherapy. Statistical methods: continuous variables analysed using independent samples *t*-test; categorical variables analysed using χ^2-test; $P < 0.05$ significant. [a]Owing to small cell size; combined oropharynx and nasopharynx. [b]Owing to small cell size; combined T0 and Tx; combined recurrent and other. [c]Owing to small cell size; combined other and unknown. [d]Owing to small cell size; combined radiotherapy alone and chemotherapy alone. Adapted from Brown *et al.*[18] (copyright © 2012 Wiley Periodicals, Inc.).

87% in the original cohort for validation). Of the 88 high-risk patients, 89% (*n* = *78*) received a proactive gastrostomy as per the protocol recommendation (Figure 3). Only three of these patients ended up not meeting the final criteria for proactive gastrostomy, as they did not use their tube and had < 10% weight loss. Two patients did not use their tube against recommendations and thus lost > 10% weight. All other patients used their tube. A proactive gastrostomy was not placed in the remaining 10 high-risk patients because the procedure was medically contraindicated (*n* = 1), was refused by the patient or treating consultant (*n* = 2) or other reasons such as scheduling difficulties (*n* = 7). Six of these patients did end up meeting the final outcome criteria for proactive gastrostomy insertion based on their individual outcomes (Figure 3). Of the 182 non-high-risk patients, 8 did have a proactive gastrostomy tube inserted, despite no recommendation in the protocol. Seven of these patients did use their tube (one patient had > 10% weight loss despite tube use), and therefore selection for placement was deemed appropriate. Only one patient did not use the tube and was able to minimise weight loss to < 10%. Of the remaining 174 low-risk patients without a tube, three patients had a gastrostomy placed during treatment, three patients had a nasogastric tube for > 4 weeks and 19 patients had > 10% weight loss. Therefore, in total 25 patients did end up meeting the final outcome criteria for proactive gastrostomy insertion based on their individual outcomes.

Validation of the protocol

Of the 270 patients, 113 (42%) met the predefined positive prediction 'did need a proactive gastrostomy' based on patient outcomes. Of these, 32 patients (28%) failed to be identified as

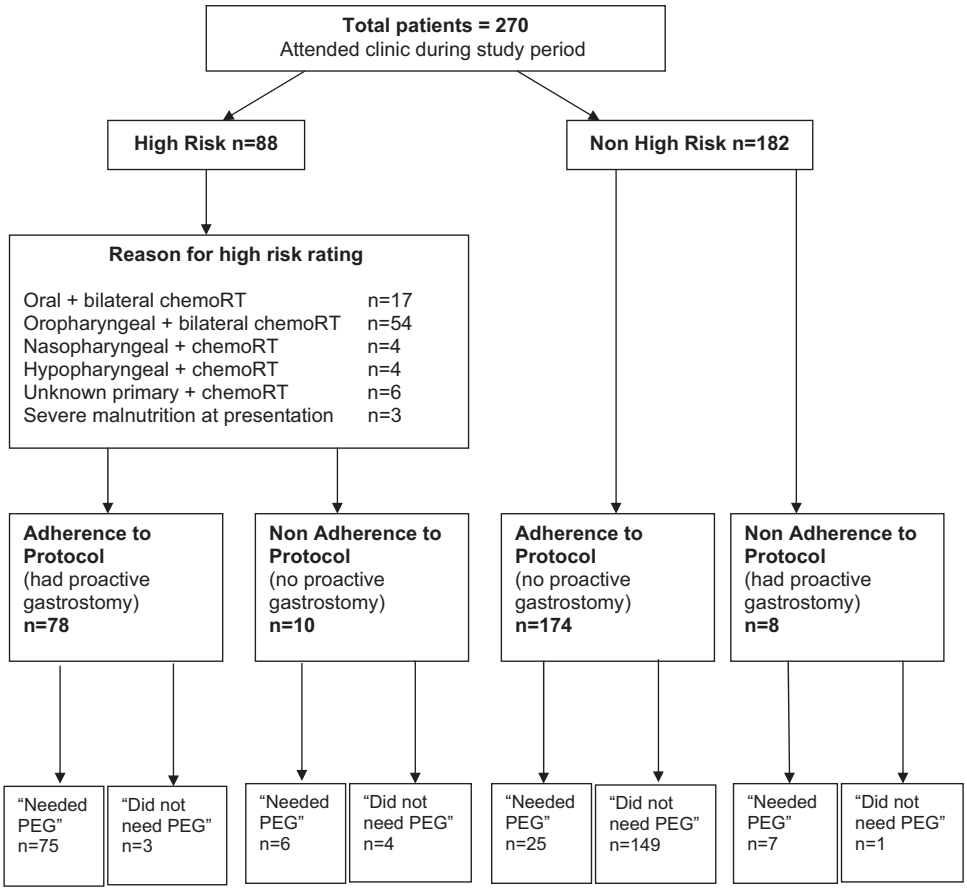

Figure 3. Adherence to the Royal Brisbane and Women's Hospital Protocol for the swallowing and nutrition management of patients with head and neck cancer and associated outcomes. Abbreviations: chemoRT, chemoradiotherapy; PEG, percutaneous endoscopic gastrostomy; NGT, nasogastric tube.

Table 2. Method of nutrition support utilised during treatment in the 2010–2011 patient cohort

Type of nutrition support	*Total patients* (n = *270*)	*Frequency (%)*
Nil tube feeding	170	63
Proactive gastrostomy tube[a]	86	32
Used	80	93
Unused	6	7
Reactive tube	14	5
NGT < 4 weeks	5	36
NGT > 4 weeks	3	21
NGT and PEG	3	21
PEG	3	21

Abbreviations: NGT, nasogastric tube; PEG, percutaneous endoscopic gastrostomy tube. [a]Proactive gastrostomy tube indicates therapeutic or prophylactic gastrostomy placed prior or within first 2 weeks of treatment.

high risk using the protocol. An exploration of this group was undertaken to see whether any common factors could be identified. Overall seven patients had surgery alone, and all others had unilateral radiotherapy (either adjuvant or definitive ± chemotherapy). There were seven patients the consultants identified for proactive gastrostomy, which were mainly T3, T4 or N2 staging ($n = 5$) and oral cavity tumours ($n = 5$). There were seven patients who required a reactive feeding tube, four of whom had surgery alone, but otherwise there were no other common factors with site or staging. The remaining 18 patients who all lost > 10% body weight had no other common sites, but the majority had T3, T4 or N2 staging ($n = 10/18$).

Of the 270 patients, the remaining 157 patients, all of whom lost < 10% body weight, met the predefined alternative patient outcome 'did not need a proactive gastrostomy'. Of these, seven (4%) patients were identified as false positives (that is, a result that indicates the patient is high risk when they are not). Therefore, sensitivity of the protocol risk categories to predict patients' need for a proactive gastrostomy was 72%, specificity was 96%, positive predictive value was 92% and negative predictive value was 82% (Table 3).

DISCUSSION

This study aimed to validate the updated protocol for the swallowing and nutrition management of patients with head and neck cancer in relation to the new high-risk category definition for proactive gastrostomy insertion. The study was undertaken in a new cohort, with patients receiving standard 3-D conformal radiotherapy and H-IMRT. Compared with data collected in the validation of the original protocol where patients only received 3-D conformal radiotherapy,[18] this study found that both the sensitivity and specificity improved and that indication for proactive gastrostomy using the updated high-risk category definition was appropriate.

The increased sensitivity of 72% (compared with previous results of 54%) meant that there was a lower percentage of false negatives and more patients were likely to be correctly identified for a gastrostomy when required. When the characteristics of the

Table 3. Sensitivity and specificity of the risk categories in the Royal Brisbane and Women's Hospital Protocol for the swallowing and nutrition management of patients with head and neck cancer to predict requirement for proactive gastrostomy insertion in a mixed cohort of patients receiving 3-D conformal radiotherapy and Helical-IMRT

	Prediction for proactive gastrostomy[a] defined from patient outcomes at end of acute cancer treatment		*Positive and negative predictive values*
	Positive: did need a proactive gastrostomy[b] (n)	*Negative: did not need a proactive gastrostomy[c] (n)*	
Determined from protocol risk criteria			
High risk[d]	81 (TP)	7 (FP)	PPV = TP/(TP+FP) 92%
All other patients[e]	32 (FN)	150 (TN)	NPV = TN/(FN+TN) 82%
Sensitivity and specificity	Sensitivity = TP/(TP+FN) 72%	Specificity = TN/(FP+TN) 96%	

Abbreviations: FN, false negative; FP, false positive; IMRT, intensity modulated radiotherapy; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive. [a]Proactive gastrostomy indicates therapeutic or prophylactic gastrostomy placed prior or within first 2 weeks of treatment. [b]Positive prediction = met the predefined primary patient outcome. 'A patient did not have an active gastrostomy or long-term NGT and had $\geqslant$10% weight loss or a patient had an active gastrostomy or long-term NGT'. [c]Negative prediction = met the predefined alternative patient outcome. A patient did not have an active gastrostomy or long-term NGT and had $<$10% weight loss. [d]Recommended for proactive gastrostomy insertion. [e]No recommendation for proactive gastrostomy insertion.

false negatives were investigated to see whether any improvements could be made to the guidelines, advanced staging (such as T3 and T4) appeared to be an important factor to consider, which is also widely supported in the literature.[5,32,33] A number of patients also received surgery alone or post-operative radiotherapy, and hence more consideration should perhaps be given to the surgical procedure. Other guidelines have since been developed specifically for this,[33] and they could be used to further inform decision making in this population.

The specificity remained high at 96% (compared with previous results of 93%), indicating a lower percentage of false positives, and fewer patients were likely to receive a gastrostomy unnecessarily. The improvement in the sensitivity and specificity compared with the previous study is attributed to the minor changes to the criteria used to identify high-risk patients in the protocol (Figure 1) and the clinical and treatment differences noted between the cohorts, which may possibly be explained by the increasing incidence of HPV oropharyngeal tumours.[24]

In regard to the advances in treatment techniques over time, research relating specifically to H-IMRT and its impact on nutrition outcomes and tube feeding requirements is sparse, with the majority of the studies to date reporting on outcomes following linear accelerator-based IMRT. Long-term benefits following IMRT are well documented with reduced xerostomia and improved quality life, due to reduced radiation dose to the parotid glands.[34] Because of the reduced dose-volume achieved with IMRT some authors have postulated that this may lead to a reduced need for a gastrostomy when treated with IMRT alone.[35] However, there are studies that also continue to support the role of a proactive gastrostomy with IMRT, particularly with concurrent treatment,[36] and rates of gastrostomy dependence have not been found to be any different with IMRT.[37]

Several studies suggest that H-IMRT can achieve superior dose sparing to organs at risk versus other forms of IMRT,[23,38–40] strengthening the rationale that intensive nutrition support with a feeding tube may no longer be warranted with this advanced treatment technique. However, there are very limited data on the usage of feeding tubes with H-IMRT. In one small study ($n=5$), all patients had a proactive gastrostomy tube placed; however, nutritional outcomes or tube use was not reported.[41] Another small study ($n=17$) reported that no patients in their case series received a gastrostomy; however, 29% ($n=5$) had severe weight loss $>$10%.[42]

Weight loss secondary to acute radiation toxicity is a well-recognised side-effect of radical treatment for head and neck cancer,[43] and a number of studies support that weight loss is a recurring problem with H-IMRT.[22,44,45] Similarly, we found that 64% of patients experienced clinically significant weight loss during treatment; 46% (123/270) lost $\geqslant$5 and 18% (49/270) lost $\geqslant$10% of their body weight. Of the patients who received H-IMRT ($n=75$), 25% lost $\geqslant$5 and 23% lost $\geqslant$10%. Weight loss remains prevalent, despite advances in treatment techniques,[46] and therefore nutrition support is essential to assist with maintaining nutritional status, which has been shown to improve quality of life[47,48] and other clinical outcomes.[49] The protocol for proactive gastrostomy placement hence remains just as relevant for advanced techniques of radiation treatment delivery.

There are limitations in the interpretation of these results because of the study being undertaken at a single site and therefore limiting the applicability to other centres not using the protocol. The retrospective study design also results in a number of patients being excluded because of access issues to the medical chart and missing outcome weight data. There was a smaller sample size compared with the previous cohort used (1-year versus 2-year data collection), and the study only had a small subset of radiotherapy patients who actually received H-IMRT (75/230). This introduced some selection bias as patients were generally prioritised for H-IMRT if they had extensive fields, high-risk tumour sites such as the base of tongue or required bilateral irradiation rather than ipsilateral irradiation.

The strength of this study is the favourable sample size compared with other published studies to date that have reported on nutrition outcomes and tube feeding requirements with H-IMRT, which therefore helps develop our knowledge in this field. Studies with IMRT have shown median gastrostomy use of 3 months[50] and benefits in expediting gastrostomy removal with the dose constraints formulated during planning;[51] however, we do not fully understand the impact of H-IMRT on the duration of gastrostomy use. According to the evidence-based European Society of Clinical Nutrition and Metabolism non-surgical oncology guidelines,[52] a nasogastric tube is recommended for nutrition support that is required for $<$4 weeks, and therefore this may be a more appropriate method of tube feeding if indeed the duration of gastrostomy use is $<$4 weeks. Therefore, determining the duration of gastrostomy use will be an important consideration in future studies with H-IMRT.

In summary, the results of this study confirm that the protocol's updated high-risk category is valid to predict proactive gastrostomy placement with a higher sensitivity and specificity.

The revised version is therefore preferable for clinical use and has been shown to be appropriate for a mixed patient cohort receiving both 3-D conformal radiotherapy and H-IMRT.

CONFLICT OF INTEREST

TB received a Royal Brisbane and Women's Hospital PhD Scholarship. The funding body was not involved in the study design, data collection, analysis and interpretation of results, writing of the report or the decision to submit the article for publication. The remaining authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

TB initiated the study concept. TB, JB, MB and BH contributed to study design. VG, TB and CL participated in the acquisition of data. VG and TB analysed the data, and VG prepared the first draft of the manuscript. All the authors participated in the interpretation of the data, critical revision of the manuscript and the final approval of the submitted version. As corresponding author TB has full access to all the data in the study and has final responsibility for the decision to submit for publication.

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