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RESEARCH ARTICLE

Multimodal cancer treatment and its association with nutrition care practices in patients with head and neck and esophageal cancer: an international prospective cohort study

Leah Gramlich[1*], Rupinder Dhaliwal[2], Narisorn Lakananurak[3], Vickie Baracos[4], Merran Findlay[5], Judith D. Bauer[6], Marian de van der Schueren[7], Alessandro Laviano[8], Adrianne Wideman[9], Andrew G. Day[10], Lisa Martin[11].

[1]Department of Medicine, University of Alberta, Canada
[2]Canadian Nutrition Society, Ottawa, ON K1C 6A8, Canada
[3]Division of Clinical Nutrition, Department of Medicine, Chulalongkorn University, Bangkok, Thailand, 10300
[4]Department of Oncology, Cross Cancer Institute, University of Alberta, Edmonton, AB T6G1Z2, Canada
[5]Cancer Services, Royal Prince Alfred Hospital, Camperdown, NSW 2050, Australia; Chris O'Brien Lifehouse, Camperdown, NSW 2050, Australia; Cancer Care Research Unit, Susan Wakil School of Nursing and Midwifery, Faculty of Medicine and Health, University of Sydney, Camperdown, NSW 2050 Australia; Maridulu Budyari Gumal (SPHERE) Cancer Clinical Academic Group, South Western Sydney Clinical School, University of New South Wales, Sydney, NSW 2052, Australia
[6]Department of Nutrition, Dietetics and Food, Monash University, Clayton, Victoria, Australia
[7]Department of Nutrition, Dietetics and Lifestyle, School of Allied Health, HAN University of Applied Sciences, 6503 GL Nijmegen, The Netherlands; Department of Human Nutrition and Health, Wageningen University and Research, 6700 AA Wageningen, The Netherlands
[8]Department of Translational and Precision Medicine, Sapienza University of Rome, I-00185 Rome, Italy
[9]Department of Nutrition, Food Science and Packaging, San Jose State University, San Jose, CA 95192, USA; University of California Davis Medical Center, Sacramento, CA 94558-5004, USA
[10]Department of Public Health Sciences, Queens' University, Kingston Ontario, Canada
[11]Department of Oncology, Cross Cancer Institute, University of Alberta, Edmonton, AB T6G 1Z2, Canada.

*lg3@ualberta.ca

ABSTRACT

Background: Both cancer and its' treatment contribute to the development of malnutrition, particularly in cancers that impact nutrition intake such as head and neck (HNC) and esophageal (EC) cancers. This study was undertaken to explore the relationship between cancer treatment and nutrition care in patients with HNC and EC.

Methods: Adult patients (≥18 years) with newly diagnosed head and neck (HN) or esophageal (ESO) cancers scheduled to receive cancer treatment were enrolled between 2016 and 2018 in the INFORM study, a longitudinal multi-centre prospective cohort study. Baseline clinical characteristics of patients, cancer characteristics, treatment type (chemotherapy/radiotherap y /surgery) and frequency, nutrition risk (Patient Generated Subjective Global Assessment Short Form (PG-SGA SF) and nutrition care were recorded.

Results: 100 HNC and 51 EC patients were included. Data were collected across 4 time periods from baseline to 6 months at 11 sites in Canada, Australia Italy, The Netherlands and the United States. Seventy-nine percent of the patients were male with a mean (SD) age of 63 (10) years. At admission, the mean (SD) BMI was 27 (5) kg/m2 and 30% were current smokers. Baseline PGA-SGA SF was ≥ 4 indicating nutrition risk for 59% of the HNC and 77% of the EC patients. The number of cancer treatments was positively associated with increases in enteral (EN) and parenteral nutrition (PN). In HNC patients receiving a single cancer treatment, 39% required EN and with 3 cancer treatment types, 78% required EN. In EC requiring a single cancer treatment, 50% required EN and in patients with 3 cancer treatments 94% required EN.

Conclusion: The number of cancer treatment modalities is associated with the intensity of nutrition therapy required to sustain the patients through their cancer journey.

Keywords: nutrition care, head and neck cancer, esophageal cancer, cancer treatment.

Introduction

The relationship between malnutrition and poor outcome in patients with cancer is well described[1]. Patients undergoing multimodal cancer treatment, inclusive of surgery, chemotherapy and/or radiation therapy, are at risk for developing malnutrition due to both their cancer and its treatment[2]. Different cancers are associated with variable impact on nutrition risk. Two cancers associated with the highest risk of malnutrition include Head and Neck cancer (HNC) and Esophageal cancer (EC)[3], related to the nutrition impact symptoms, tumor related changes in metabolism and to the multimodal care required for treatment. The prevalence of malnutrition at diagnosis ranges from 30% to 77% in patients with HNC[4-7] and from 57% to 80% in patients with EC[8,9].

Malnutrition is associated with poor clinical outcomes in HNC and EC patients, including increased risk of infection, impaired wound healing, muscle weakness, poor quality of life, increased length of hospital stay, and increased mortality rate[10-13]. In addition, malnutrition may result in treatment interruption and reduced response to chemotherapy and radiotherapy[14]. Given the site of foregut tumors, dysphagia is reported in 18% to 94% of HNC patients 8% and 90% of EC patients, contributing to malnutrition[6,9]. Although multimodal treatments result in improved tumor control, their side effects may result in further deterioration of nutrition status and critical weight loss of > 5%. Surgical resection has two main impacts. Alteration of anatomy may have significant consequences on a patients' ability to eat and swallow. In addition, in patients undergoing surgery, the acute surgical insult accelerates catabolism and tissue breakdown in patients who may already be at nutrition risk. Common side effects of chemotherapy and radiotherapy include anorexia, mucositis, xerostomia, altered taste and smell, and/or chewing and swallowing problem[7,10,11]. These complications can limit oral intake and lead to further weight loss throughout the patients' cancer care journey[12,13,14] which extends over a period of several months.

We wanted to understand the relationship between real-world cancer treatment patterns (chemotherapy, radiation therapy, surgery, multimodal therapy) and nutrition care processes (inclusive of screening and assessment, quality nutrition care and nutrition evaluation and monitoring)[15,16] in patients with HNC and EC, viewed through an international lens[17]. The relationship between cancer treatment patterns and nutrition care at the system level has not been well described in previous studies[18,18,19]. The aim of this study is to describe cancer treatment patterns and evaluate the relationship between cancer treatment modalities and current nutrition care practices in high nutrition risk cancers, HNC and EC, based on a 'real world' observational study of patients across 11 cancer care settings around the world.

Methods

STUDY DESIGN AND PATIENTS:

The International audit of Nutrition care in patients with FORegut tuMors (INFORM) (Clinicaltrials.gov identifier: NCT0282948) is a multi-centre prospective cohort study that was undertaken at 11 cancer care settings including in Canada (n = 6 from two cities), Australia (n = 2), Italy (n = 1), the Netherlands (n = 1) and the United States of America (USA), (n = 1) between 2016 and 2018. Participating sites were teaching hospitals required to have a registered dietitian, clinical nutritionist or nutrition delegate available for study co-ordination. Individual sites used quota sampling and recruited up to 20 participants per site. The primary purpose of this audit was to describe both current nutrition care practices (based on best available evidence from evidence based guidelines (EBG's)[15] and cancer care processes and treatments across various settings. As such, this study was not undertaken to look at specific oncologic and nutrition treatment or impact on outcome of individuals with HNC and EC.

Participating cancer centers were recruited through our existing network of practitioners with a focus on tertiary referral centers that routinely manage high volumes of patients undergoing treatment for complex, high-nutritional risk cancers spanning inpatient, outpatient and or community settings and Participating centers had a track record of a systematic approach to nutrition care processes supporting adaptation to local context and continuity of care. A full description of the participating centers' characteristics, interest in systematic approaches to nutrition care processes adapted to local context, ensuring the continuity of and adherence to EBGs for nutrition care has been published [17]. Patient inclusion criteria were adult (≥18 years) patients with a diagnosis of HNC or EC commencing treatment (any modality) of curative intent. Exclusion criteria were either absence of a treatment plan due to imminent death or an Eastern Co-operative Oncology Group (ECOG) [38] score ≥ 4.

Approvals from the Health Research Ethics Board at the University of Alberta (Pro00060716) and at all participating site ethics review boards were obtained. (HREBA-CC; Approval Code: HREBA.CC-15-0238. Approval Date: February 2, 2016).

DATA COLLECTION:

Baseline clinical characteristics of patients including age, sex, type and stage of cancer were recorded. Type (chemotherapy, radiotherapy, surgery) and frequency of cancer treatment received was collected prospectively from baseline (time 0) to 2 months (time 1), 4 months (time 2) and at 6 months (time 3) over the study period. Specific data related to the duration of EN and PN was not captured. The Patient Generated Subjective Global Assessment Short Form (PG-SGA SF) is a validated self-report nutrition risk screening tools for use in oncology settings that was by completed by patients at baseline and at 2, 4 and 6 months. The PG-SGA SF[20] has been validated against Subjective Global Assessment (SGA)[21] and has been accepted as the standard for nutrition assessment for patients with cancer by the Oncology Nutrition Dietetic Practice Group of the American Dietetic Association. It consists of a single-page nutrition risk screening questionnaire that asks patients to reflect on changes in four domains: their body weight (Box 1), their food intake (Box 2), symptoms impacting their ability to eat (Box 3), and their current activity and function level (Box 4). The box scores from each section are summed to yield a total score (range 0 to 37). The level of nutrition risk is pre-determined according to nutrition triage recommendations embedded within the PG-SGA SF tool: scores 0–1 (no intervention, reassess regularly), scores 2–3 (patient and family education by appropriate healthcare provider; pharmacological intervention as indicted by symptoms), scores 4–8 (intervention by a registered dietitian in conjunction with nurse or physician as indicated by symptoms), scores ≥9 (critical need improved symptom management and nutrition intervention options. Patients were classified at nutrition risk if their score was ≥4 [22], according to the triage recommendations, which align with the Nutrition Care Process. Details on the nutrition care received were obtained by a dietitian/delegate at baseline (i.e., the first time the patient was introduced to the Cancer Care System i.e. clinic or hospital) and then every time the patient was seen by the dietitian/delegate throughout the 6 month study period. These data included type and routes of nutrition (oral diet, oral nutrition supplements (ONS), enteral nutrition (EN), parenteral nutrition (PN), timing of nutrition support (EN or PN), and percent of target energy and protein goals received. Requirement for escalating intensity of nutrition therapy from oral diet, to the use of ONS to EN and to PN was recorded.

Research Electronic Data Capture (REDCap)[23,24] hosted at the University of Alberta, Canada, was used to capture data collected at each participating site from electronic and paper-based electronic medical records.

STATISTICAL ANALYSIS:

All variables were described separately (HNC or EC). Categorical variables were reported as counts and percentages while continuous variables were reported as means with standard deviations. This analysis is primarily descriptive as driven by our study goals and design. The Mantel-Haenszel test for linear trend was used to test if an increasing number of cancer treatment modalities (oncologic modalities) was associated with the intensity of nutrition therapy, ranging from low to high: oral only without supplements<oral with supplements only<EN without PN<PN with or without EN. The statistical analysis was performed using SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

INFORM COHORT CHARACTERISTICS:

One hundred and seventy patients (119 HNC and 51 EC) were enrolled between 2016 and 2018 in the INFORM study. We excluded all 19 patients from one site (Sapienza, Rome; all HNC) that did not collect information on cancer treatment leaving 100 HNC and 51 EC patients in the current analysis. Table 1 reports the baseline characteristics of the cohort. Of the 151 participants, 119 (79%) were male with a mean (standard deviation) age of 63 (10) years. At admission, the mean (SD) BMI was 27 (5) kg/m^2 and 30% were current smokers. Performance status based on ECOG score at the outset of treatment indicates the majority of patients were fully active (ECOG 0: 70%) or restricted in physically strenuous activity but were ambulatory and able to carry out light activities (ECOG 1: 25%) and findings were similar between HNC and EC. Patients with HNC reported greater use of alcohol than those with EC (44% vs. 18%). The most common location for HNC was oropharynx cancer (37%) followed by oral cavity (23%) and laryngeal cancer (16%). Patients with EC had predominantly adenocarcinoma (80%). Patients with HNC tended to present with more advanced disease (5% with stage I, 8%

stage II, 43% with stage IV disease) than those with EC (8% stage I, 25% stage II, 29% stage III). Amongst this cohort, 95% of the HNC patients and 92% of the EC patients received cancer treatment. The vast majority (87%) of patients received cancer treatment as an outpatient.

Table 1: Baseline characteristics of the INFORM study population

		Head and Neck Cancer (n=100)	Esophageal Cancer (n=51)	All (n=151)
Centre				
	Calgary	21 (21%)	10 (20%)	31 (21%)
	Chris O'Brien Lifehouse	20 (20%)	0	20 (13%)
	Edmonton	20 (20%)	18 (35%)	38 (25%)
	Netherlands	20 (20%)	23 (45%)	43 (28%)
	RBWH Brisbane	10 (10%)	0	10 (7%)
	UC Davis	9 (9%)	0	9 (6%)
Age		62.1±9.9	63.7±10.2	62.6±10.0
Sex				
	Male	78 (78%)	41 (80%)	119 (79%)
	Female	22 (22%)	10 (20%)	32 (21%)
Ethnicity				
	White	94 (94%)	50 (98%)	144 (95%)
	Asian	2 (2%)	1 (2%)	3 (2%)
	First Nations	1 (1%)	0	1 (1%)
	Hispanic	1 (1%)	0	1 (1%)
	East Indian	1 (1%)	0	1 (1%)
	Other	1 (1%)	0	1 (1%)
Body Mass Index (BMI)		26.9±5.5	27.8±4.7	27.2±5.3
Current Smoker		33 (33%)	13 (25%)	46 (30%)
Alcohol use		44 (44%)	9 (18%)	53 (35%)
ECOG				
	0	74 (74%)	32 (63%)	106 (70%)
	1	21 (21%)	16 (31%)	37 (25%)
	2	3 (3%)	3 (6%)	6 (4%)
	3	2 (2%)	0	2 (1%)
TNM stage of cancer				
	I	5 (5%)	4 (8%)	9 (6%)
	II	8 (8%)	13 (25%)	21 (14%)
	III	17 (17%)	15 (29%)	32 (21%)
	IV	-	4 (8%)	4 (3%)
	IVa	43 (43%)	-	43 (28%)
	IVb	9 (9%)	-	9 (6%)
	IVc	4 (4%)	-	4 (3%)
	Missing	-	2 (4%)	2 (1%)
	NA	7 (7%)	9 (18%)	16 (11%)
	NS	7 (7%)	4 (8%)	11 (7%)
Location of the patient at baseline				
	Inpatient	14 (14%)	4 (8%)	18 (12%)
	Outpatient	85 (85%)	47 (92%)	132 (87%)
	Over the phone	1 (1%)	0 (0)	1 (1%)

INFORM COHORT: NUTRITION RISK:

A significant proportion of both HNC and EC patients were identified as at nutrition risk based on PG-SGA SF ≥4. At baseline PG-SGA SF was ≥ 4 for 59% of the HNC patients and by 4 months 72% had PG-SGA≥4. In EC patients 77% had baseline PG-SGA SF ≥ 4 and by 4 months the corresponding numbers were 84% in those with scores completed (supplemental table 2 reports the percentage of patients with PG-SGA SF ≥ 4 overall and by cancer treatment modality). Figure 1 depicts the percentage of patients with PG-SGA SF ≥ 4 over time by number of cancer treatment modalities and cancer type. In both HNC and EC, patients incurred weight loss between time of presentation and completion of cancer treatment. Specifically, the 73 head and neck and 36 esophageal cancer patients with baseline and 6-month weight recorded, lost a mean(SD) of 9.4 (9.5)% and 9.1 (7.6)% of their baseline weight on average by six months. This weight loss was largely driven by reduction in oral intake related to nutrition impact symptoms (data not shown).

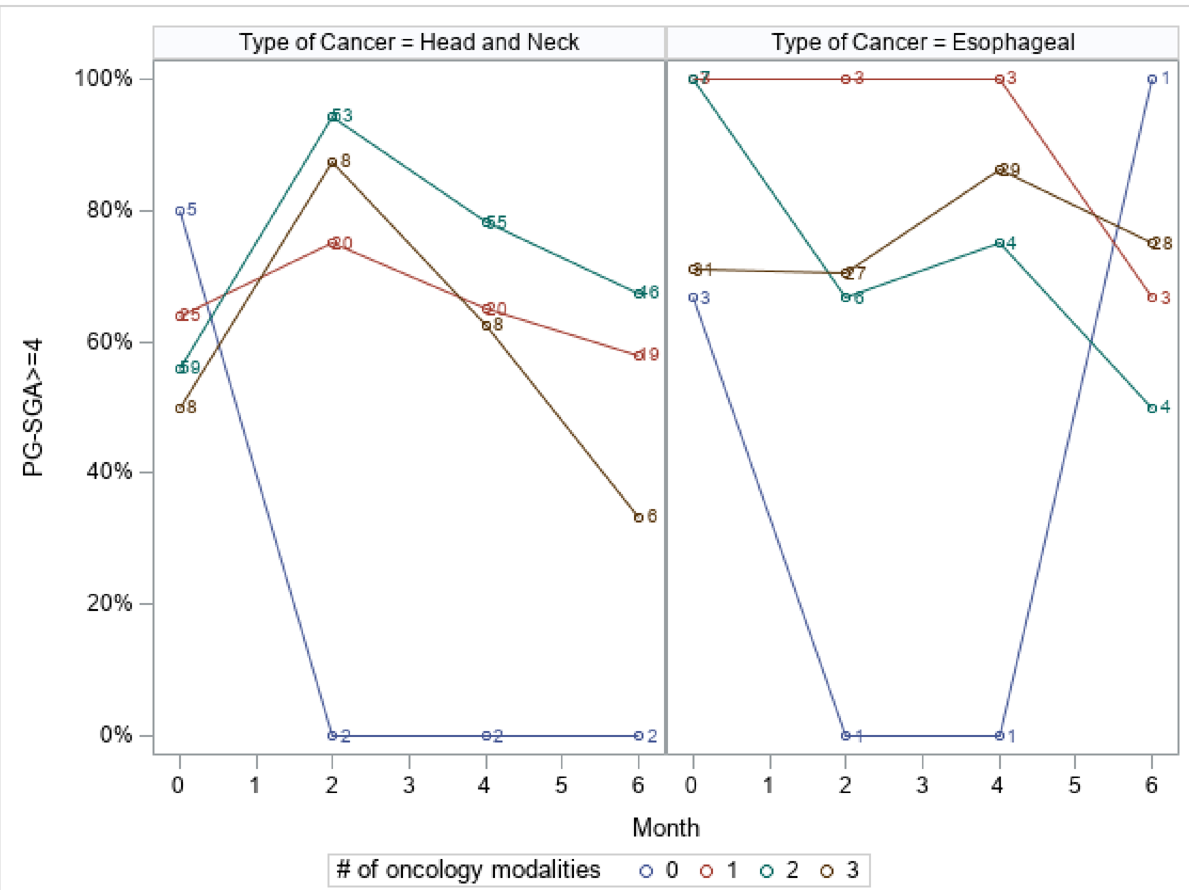


Figure 1: Percentage of INFORM patients with PGSGA>4 and number of cancer treatments

This figure is generally representative of cancer treatment patterns and approaches in both HNC and EC. HNC patients were most likely to have combined therapy with chemotherapy and radiation therapy with peak symptoms at month 2-3. In contrast, patients with EC may have had neoadjuvant chemoradiation with a surgical intervention around month 3-4.

CANCER TREATMENT PATTERNS AND NUTRITION CARE PROCESSES:
Table 2 illustrates the number of cancer treatment modalities and route of nutrition therapy. Oral nutrition supplements were frequently prescribed and used by patients. The number of cancer treatments was positively associated with increases in non-volitional feeding including enteral and parenteral nutrition (EN, PN). Patients who were treated with three cancer treatment modalities (chemotherapy, radiotherapy, surgery) were most likely to require and receive EN to support their nutrition status. In HNC patients receiving a single cancer treatment, 39% required EN and with 3 cancer treatment types, 78% required EN. In EC requiring a single cancer treatment, 50% required EN and in patients with 3 cancer treatments 94% required EN. In patients with HNC, EN was provided by percutaneous gastrostomy tubes alone whereas in EC, EN was provided by a variety of enteral access devices including gastrostomy tubes (EN Gastric), and by other enteral routes including naso-enteric feeding and jejunal tubes. PN was not frequently used (1% in HNC, 6% in EC (not significantly different)). Data regarding absolute duration of EN and PN was not captured. Although the route of nutrition prescribed (oral, oral plus ONS, EN, PN) to patients with HNC and ECA helped patients treated with multiple oncologic modalities to get closer to their target nutritional intakes, these targets were not met and additional weight loss was incurred by both HNC and ECA groups at six months (figure 1).

Table 2: Nutrition therapy and cancer treatment in INFORM study population

		Head and Neck (n=97)			Esophageal (n=51)		
Nutrition Treatment	Route	n total	n received	%	n total	n received	%
Cancer Treatment							
Chemotherapy alone	ONS	0	0	-	2	2	100%
	EN	0	0	-	2	0	0%
	PN	0	0	-	2	0	0%
	EN Gastric	0	0	-	2	0	0%
Chemotherapy with surgery	ONS	0	0	-	1	1	100%
	EN	0	0	-	1	1	100%
	PN	0	0	-	1	0	0%
	EN Gastric	0	0	-	1	0	0%
None	ONS	4	3	75%	4	2	50%
	EN	4	0	0%	4	0	0%

		Head and Neck (n=97)			Esophageal (n=51)		
Nutrition Treatment	**Route**	**n total**	**n received**	**%**	**n total**	**n received**	**%**
	PN	4	0	0%	4	0	0%
	EN Gastric	4	0	0%	4	0	0%
Radiotherapy alone	ONS	15	11	73%	0	-	-
	EN	15	4	27%	0	-	-
	PN	15	0	0%	0	-	-
	EN Gastric	15	4	27%	0	-	-
Chemoradiotherapy	ONS	54	48	89%	7	5	71%
	EN	54	34	63%	7	5	71%
	PN	54	0	0%	7	1	14%
	EN Gastric	54	34	63%	7	4	57%
Chemoradiotherapy with surgery	ONS	9	7	78%	35	33	94%
	EN	9	7	78%	35	24	69%
	PN	9	0	0%	35	1	3%
	EN Gastric	9	7	78%	35	6	17%
Radiotherapy with surgery	ONS	7	5	71%	0	-	-
	EN	7	6	86%	0	-	-
	PN	7	1	14%	0	-	-
	EN Gastric	7	6	86%	0	-	-
Surgery alone	ONS	8	5	63%	2	2	100%
	EN	8	5	63%	2	2	100%
	PN	8	0	0%	2	1	50%
	EN Gastric	8	5	63%	2	2	100%

Details of cancer treatment in this HNC and EC patient cohort are described in table 3. The vast majority of patients studied received cancer treatment however, 5% of patients with HNC and 8% of those with EC did not receive treatment for their cancer.

Table 3: Cancer Treatment in patients in the INFORM population

		Head and Neck Cancer (n=100)	Esophageal Cancer (n=51)
Number of treatment modalities			
	0	5 (5%)	4 (8%)
	1	25 (25%)	4 (8%)
	2	61 (61%)	8 (16%)
	3	9 (9%)	35 (69%)

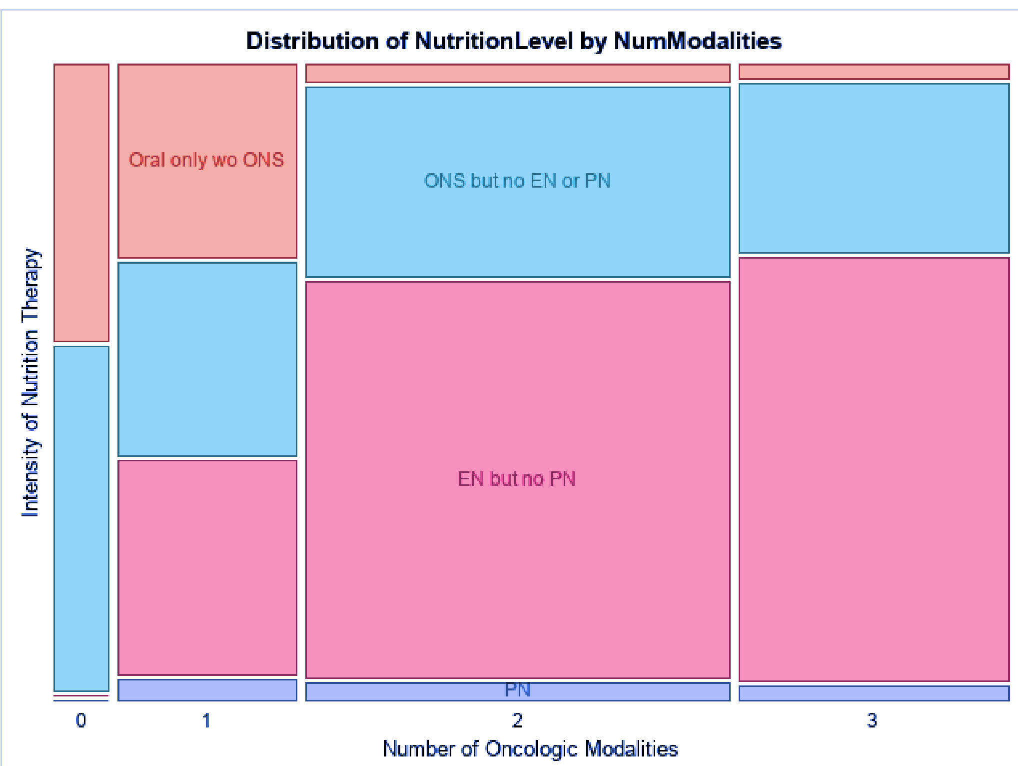
		Head and Neck Cancer (n=100)	Esophageal Cancer (n=51)
Specific type of cancer treatment			
	No treatment	5 (5%)	4 (8%)
	Chemotherapy alone	0	2 (4%)
	Radiotherapy alone	15 (15%)	0
	Surgery alone	10 (10%)	2 (4%)
	Chemoradiotherapy	54 (54%)	7 (14%)
	Radiotherapy + Surgery	7 (7%)	0
	Chemotherapy _ Surgery	0	1 (2%)
	Chemoradiotherapy + Surgery	9 (9%)	35 (69%)
Had Chemotherapy		63 (63%)	45 (88%)
Had Radiotherapy		85 (85%)	42 (82%)
Had Surgery		26 (26%)	38 (75%)
Had Esophageal Stent		-	5 (10%)
		n=84	n=42
Dose of Radiation		6535±774	4208±429

In all patients with HNC, 85% of patients had radiotherapy and 63% had chemotherapy. Surgery was undertaken in 26% of patients with HNC. However, HNC patients most commonly underwent treatment with two treatment modalities (61%), usually chemoradiotherapy, followed by single modality therapy in 25% of patients (usually radiotherapy alone).

Eighty eight percent of patients with EC had chemotherapy, 82% had radiation and 75% had surgery. Most commonly EC patients had treatment with three modalities (69%) which was always chemoradiotherapy and surgery (69%); and 16% were treated with 2 treatment modalities, usually chemoradiotherapy.

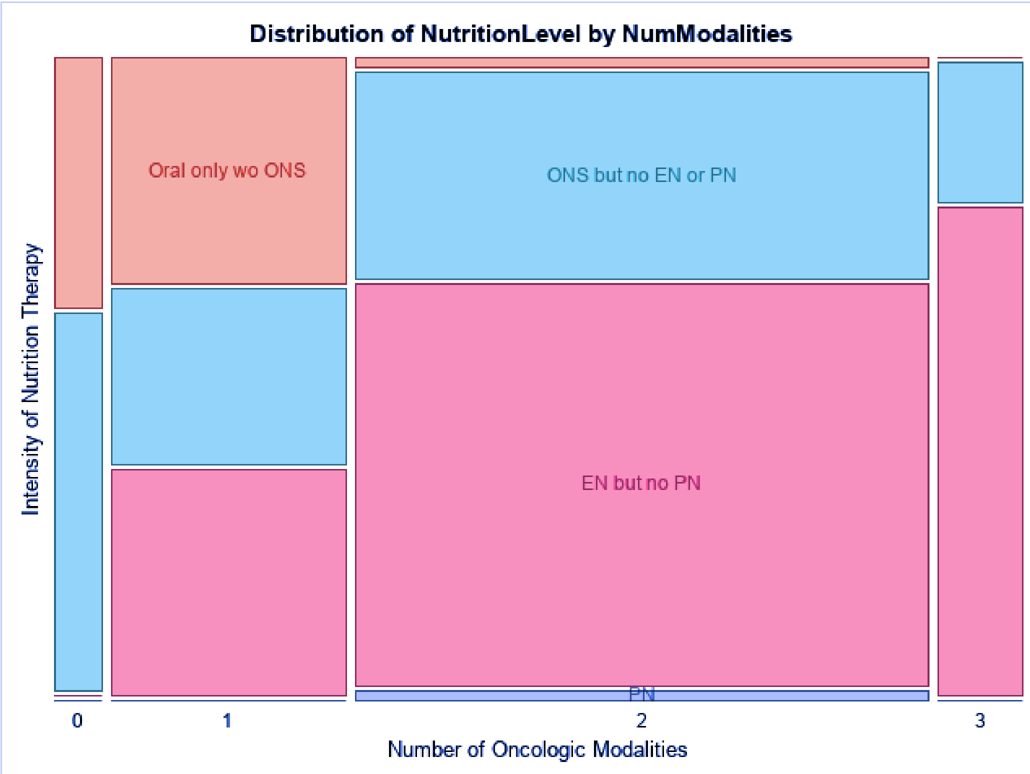
In these two unique cancer types there were more cancer treatments used in patients with EC compared to HNC (most commonly 3 vs 2) with significantly more use of surgery (75% vs 26%) and chemotherapy (88% vs 63%) in EC vs HNC. Doses of radiation were greater in HNC than in ECA (mean=6535 gy vs 4208 gy). Figures 2a, 2b and 2c examine the trend between number of Cancer Treatments (oncology modalities) and nutrition intensity where nutrition intensity is ordered as: 0-oral only, 1-ONS wo EN or PN, 2-EN wo PN and 3-had PN. There a highly significant linear trend between number of cancer modalities and nutrition intensity. Figure 2a represents the combined HNC and EC populations, 2b represents HNC and 2c represents EC. The intensity of nutrition therapy is displayed on the y-axis and distinguished by color. The intensity of nutrition therapy ranges from low intensity including oral therapy alone in orange (dietary counsel) to inclusion of Oral Nutrition Supplements (ONS) in light blue to higher intensity therapy such as Enteral (EN) in pink and Parenteral (PN) nutrition in mauve. The number of oncologic modalities ranging from 0-3 is represented on the x-axis. The width and height of the bar graphs depict the proportion of patients with the given number of oncologic modalities and nutrition intensity respectively. Thus, the area of the rectangles depicts the proportion of patients with a given combination of oncologic modalities and nutrition intensity respectively. The area of the rectangles depicts the proportion of patients with a given combination of oncologic modalities and nutrition intensity respectively. For example, in the combined HNE and EC group, most commonly patients received two cancer treatment types and required EN. Overall, for patients with HNC and EC, the more cancer treatment modalities used, the more likely the patient was to require more intensive nutrition therapy, incrementally prescribed and used, from oral therapy with dietary counsel and diet modification alone, to use of ONS, to requirement for Enteral Nutrition or Parenteral Nutrition (p-value <0.0001).

Figure 2: Intensity of Nutrition Therapy and Number of Cancer Treatments (oncologic modalities)



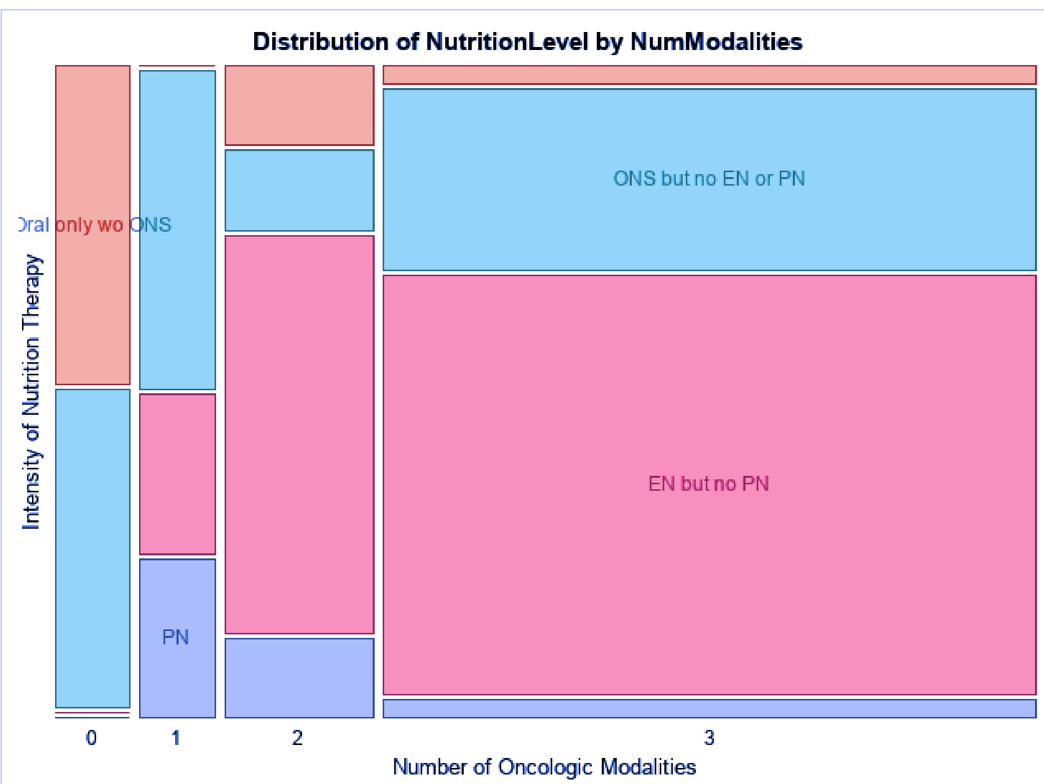
Test for linear trend between number of oncologic modalities and nutrition support intensity df=1, Chi-Square=24.9, p<0.0001

2a. Intensity of nutrition therapy and number of cancer treatments HNC and EC combined



Test for linear trend between number of oncologic modalities and nutrition support intensity df=1, Chi-Square=21.3, p<0.0001

2b. Intensity of nutrition therapy and number of cancer treatments: HNC



Test for linear trend between number of oncologic modalities and nutrition support intensity df=1, Chi-Square=5.2, p<0.023.

2c. Intensity of nutrition therapy and number of cancer treatments: EC

Discussion:

This international cohort of patients with foregut tumors allows us to study the relationship between cancer treatment and nutrition care in patients at high risk for malnutrition due to their cancer and its treatment in a real-world setting. There is a clear demonstration of the relationship between number of cancer treatments used in HNC and EC treatment and the requirement for more intensive nutrition therapy. Over half of HNC and EC patients will require enteral nutrition due to symptoms affecting food intake to support nutrition status over the course of their treatment. This is important for the medical, surgical and radiation oncologist to recognize. It is also relevant to consider that care often occurs across multiple locations across multiple care providers and disciplines over a prolonged period of time. Dietitians working within multidisciplinary oncology teams work with evidence-based guidelines to guide nutrition care. Despite provision of incremental nutrition care from diet modification alone to the use of oral nutrition supplements and enteral and parenteral nutrition, critical weight loss is still experienced by patients undergoing care[22]. Gaps in care have been demonstrated in the perioperative time period. During this time period, intake is inadequate[17]. We have identified that HNC patients experience weight loss and reduced food intake at around 2 months after the initiation of cancer treatment and EC patients experience these symptoms more between months 2-4 of treatment. These time periods represent an opportunity for more aggressive and timely provision of nutrients either orally, enterally or parenterally in patients undergoing cancer treatment. Meng et al. demonstrated that use of oral nutrition supplements for 3 months after surgery for abdominal cancer was associated with less sarcopenia and better tolerance to adjuvant chemotherapy[25].

In patients with HNC, the use of proactive vs reactive tube placement to support nutrition intake has been recommended in patients deemed at the greatest risk of becoming malnourished during cancer treatment[26]. A recent systematic review of the topic of timing (proactive vs reactive) of enteral nutrition support on outcome in HNC patients undergoing radiotherapy or chemoradiotherapy suggests that timing of EN may have little or no effect on tube feeding duration or complications[27]. It was recognized that the studies included in this work were small and heterogenous and that it warranted more investigation. Another key message is that early and frequent dietetic counselling and nutrition interventions throughout treatment and recovery are recommended to optimize outcomes[28,29].

The relatively infrequent use of parenteral nutrition in this study of patients who may have challenges with enteral or oral feeding because of anatomic changes associated with surgery for HNC and EC represents another potential window of opportunity to improve upon care. Perioperative parenteral nutrition could be considered in this setting if oral and enteral nutrition are not adequate to meet nutrient needs and given that surgery poses a catabolic challenge that is associated with increased nutrient utilization. It should be noted that the majority of the patients in this study were outpatients and PN is not feasible in this setting. In addition PN would be rarely clinically indicated when the gastrointestinal route of feeding is a viable option.

The duration of cancer care in patients with HNC and ECA spans many months and the greatest impact on nutrient intake occurs when the patient is receiving the largest burden of cancer therapy – eg. in the perioperative period, during active chemotherapy and radiation therapy. Symptoms of poor nutrient intake can persist during active therapy and can be prolonged. Focusing on times of greatest insult and inflammation due to therapy should be considered in terms of when to optimize nutrient intake through a variety of means, escalating the intensity of the nutrition intervention if the patient experiences ongoing involuntary weight loss despite current approaches. When patients with HNC and EC present to cancer centers for care as an inpatient, they warrant close monitoring of their nutrition impact symptoms and nutrient provision to address potential gaps that may promote the development of malnutrition and poorer outcome.

We have described the impact of oncologic therapy on nutrition care in a high nutrition risk cohort such as those patients with HNC and EC. Although, we cannot extrapolate these findings to other cancers, we hypothesize that patients undergoing cancer therapy, use of more treatment modalities may be associated with greater nutrition burden and requirement for more aggressive nutrition care. Nutrition should be considered not only during the catabolic crisis (during which the inflammatory response blunts the anabolic impact of nutrient provision), rather should be considered throughout the patients' cancer journey which in the case of multimodal cancer therapy for HNC and EC spans many months.

Study strengths include the international perspective related to both cancer and nutrition care focused in tertiary referral centers that routinely manage high volumes of patients undergoing treatment for complex, high-nutritional risk cancers. In addition, the majority of the cancer treatment occurred in the outpatient setting. In terms of limitations, the authors acknowledge the convenience sampling and lack of ethnic diversity in the study population may have resulted in selection bias. Despite the increasingly cultural and linguistic diversity of Western countries within which the study sites were located, the predominantly Caucasian study participants may be reflective of the challenges of recruiting cohorts that are representative of the broader population to research participation. We have not assessed the order of cancer treatments which may impact use nutrition care. In this cohort of patients, treatment delivery is very complex due to the number of modalities and we have only reported aggregate level data based on number of modalities. Selection bias may affect the generalizability of our findings but should compel consideration for proactive nutrition support during times of intense multimodal treatment. Finally, the sample size was relatively small and the 11 participating sites (of which we could use data from 10) may not be reflective of the practice at other sites around the world.

Conclusions:

For patients with HNC and ECA undergoing oncologic treatment, number of treatment modalities required for cancer care is associated with the intensity of nutrition therapy required to sustain the patients through their cancer care journey. In addition, oral nutrition supplements are commonly used but a majority of patients will require EN. Enteral and Parenteral nutrition are not widely used in the perioperative period and this may be an opportunity to optimize nutrition care.

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