Nutrition impact symptom monitoring and weight loss outcomes: a longitudinal radiotherapy study

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ABSTRACT

Objectives Nutrition impact symptoms (NIS) are associated with weight loss (WL), and decreased energy intake in cross-sectional studies. We aimed to ascertain associations between changes in NIS burden, energy intake and WL over time in patients with advanced cancer.

Methods Adult patients from an observational radiotherapy study for painful bone metastases self-reported NIS and WL using the Patient-Generated Subjective Global Assessment tool (PG-SGA) at baseline and week eight (W8). NIS burden, the sum of NIS per patient, categorised as 0, 1–2 and ≥3 with changes defined as 2-point differences from baseline to W8 were used. Energy intake was assessed by 24-hour recall interviews.

Results 111 patients (72.1%) were analysed and grouped by NIS burden; 0 NIS (44.1%), 1–2 NIS (30.6%) and ≥3 NIS (25.2%). Patients with NIS burden of ≥3 reported higher baseline WL compared with those with 1–2 or 0 NIS (46.4% vs 18.2% vs 10.2%, respectively, p=0.002). At W8, 21 patients (19%) reported improved NIS burden, accompanied by a lower proportion of severe (≥5%) new-onset WL (19% vs 42.1%) and higher energy intake (median 29.6 vs 21.2 kcal/kg) than those with worsened NIS burden (17.1%).

Conclusions NIS management may improve energy intake and prevent WL, emphasising the importance of systematic follow-up and interventions.

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WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Nutrition impact symptoms (NIS) are associated with reduced energy intake, weight loss (WL) and malnutrition in cancer patients. Data relies mostly on cross-sectional or head-and-neck cancer radiotherapy studies.
⇒ Despite international recommendations, systematic assessment of NIS and weight seldom occurs.

WHAT THIS STUDY ADDS

⇒ Our data suggest that changes in NIS impact intake, WL and malnutrition positively or negatively in a real-life cohort of patients with advanced cancer.
⇒ Improvement in NIS correlates with increased energy intake and prevents WL while worsening leads to reduced energy intake and severe WL.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our data reinforce the importance of systematic follow-up and interventions to address NIS, since their improvement may increase energy intake and prevent further WL.

BACKGROUND

Involuntary weight loss (WL) of >5% is common in cancer patients, with a prevalence of up to 34% at diagnosis[1] and to 50% in advanced stages. WL increases chemotherapy-related toxicity and worsens physical function and quality of life (QoL).[2] Even a pre-treatment WL of <5% is associated with reduced survival.[1]

WL is primarily due to low food intake with insufficient energy intake, mainly caused by anorexia due to chemosensory disturbances and treatment side effects.[3] Hence, side effects, such as pain, nausea, dry mouth, vomiting, diarrhoea and constipation, have been conceptualised as nutrition impact symptoms (NIS). More NIS are associated with higher WL

and malnutrition,[4] reduced function, impaired QoL and increased mortality.[5] However, the direct effects of NIS on energy intake in different cancer types and metastatic diseases are under-researched.

International guidelines recommend regular assessment of WL and appropriate NIS identification and treatment in all patients with cancer.[6] The use of patient-reported outcome measures (PROMs) is highly recommended[7] and linked with improved QoL and survival.[8] Nevertheless, WL and symptom assessment are often neglected in routine clinical practice, leading to malnutrition being underdiagnosed.[9]

This study aims to examine the effect of NIS changes on WL and energy intake and whether NIS improvement over time correlates with reduced WL and increased energy intake.

METHODS

This observational sub-study uses data from the Palliative Radiotherapy and Inflammation Study (PRAIS).[10] Data were collected pre-radiotherapy (RT) and 8 weeks post-RT. No interventions other than RT were planned. However, when the study team discovered that a patient reported a high symptom burden on one of the study questionnaires, appropriate interventions were initiated and documented. Complete data collection and procedures are described elsewhere.[10]

Participants and data collection

Patients with painful bone metastases undergoing palliative RT were recruited from Oslo University Hospital, Norway, 2015–2017. Inclusion criteria were age 18+ years and able to comply with study procedures, excluding those with recent RT, pathological fractures in long bones or missing data.[10]

NIS were measured using the Brief Pain Inventory and Patient-Generated Subjective Global Assessment of Nutritional Status short form (PG-SGA SF) (https://pt-global.org/pt-global/). NIS burden was calculated as the sum of NIS per patient and categorised as 0 NIS, 1–2 NIS, and ≥3 NIS. NIS change was defined as an increase or decrease of ≥2 points compared with baseline NIS burden. Skeletal muscle mass (SMM) was measured using CT scans at the third lumbar (L3) (Slice-O-Matic software (v.4.3 Tomovision, Montreal Canada). The cut-offs for reduced SMM were the ones used in the original publication from Martin *et al*.[11] Patients' nutritional status was evaluated using PG-SGA SF and the Global Leadership Initiative in Malnutrition (GLIM) criteria (https://www.espen.org/education/glim). Weight changes were categorised into stable, weight gain or WL of both <5% and ≥5%. Food intake was calculated using standardised 24-hour recall interviews and portion sizes.[12] Energy requirement for weight stabilisation was set to 30 kcal/kg/day.[6] During the 52-week follow-up period, overall survival (OS) was defined as the time from inclusion to death.

Statistics

Continuous variables were presented using median with IQR, and categorical variables with frequencies and percentages. Differences were analysed using Student's t-test, analysis of variance, Mann–Whitney or Kruskal–Wallis tests based on data characteristics and distribution. Categorical variables underwent X^2 tests or Fisher's corrections if needed. Spearman correlation and univariate linear regression explored relationships between independent variables (baseline and W8 NIS burden, NIS change) and dependent quantitative variables (baseline and W8 weight change). Patients with incomplete baseline and W8 data on energy intake were excluded (less than 2.0% of included patients had missing data on any of the other variables). Statistical significance was two-tailed, set at <0.05. All analyses were performed using STATA v14.1.

Ethical considerations

The Regional Committee for Medical and Health Research Ethics, Central Norway, approved the PRAIS study and amendment (2013/1126/REK Middle Norway). Written informed consent was collected. The study adhered to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline for Good Clinical Practice and the World Medical Association Declaration of Helsinki (1964).

RESULTS

Overall, 180 patients were enrolled. At W8, 24 patients had died (median OS: 5.8 weeks), 2 were lost to follow-up, and 43 did not complete the 24-hour dietary recalls, leaving 111 patients with complete baseline and W8 data on energy intake (72.1%). About 58% were men, mean Karnofsky performance status was 73.5 (SD 9.3), and prostate (27.9%), breast (27.0%) and gastrointestinal (22.0%) cancers were most prevalent. Nearly 80% received multiple fraction RT. Pain medication usage included opioids (70.3%), corticosteroids (37.8%) and nonsteroidal anti-inflammatory drugs (13.5%). Unscheduled symptom interventions (eg, opioid management, laxatives) were performed in 63.1% of patients based on baseline PROMs.[13]

At baseline, 67.6% had PG-SGA scores of ≥3 indicative of malnutrition risk, while 48.6% were moderately (36.9%) or severely (11.7%) malnourished per GLIM criteria. The most frequent NIS were anorexia (29.7%), feeling full (22.5%) and nausea (19.8%). The NIS distribution was 0 NIS (44.1%), 1–2 NIS (30.6%) and ≥3 NIS (25.2%). Among those with ≥3 NIS, 67.8% were malnourished compared with 30.6% among those with 0 NIS ($p<0.001$). Severe WL (≥5%) increased with a higher level of NIS; 0 NIS (0 %), 1–2 NIS (3.0%) and ≥3 NIS (25.0%).

At the W8 follow-up, 19.1% reported improved NIS burden, with a reduction in all symptoms. Younger women with poor baseline nutritional status, breast

Table 1 Comparison between weight change (%), energy intake and reported intake at baseline and W8, stratified by changes in nutrition impact symptoms (NIS) burden. Improved NIS burden = ↓ ≥2 points, stable NIS burden = ± 1 point change and worsened NIS burden = ↑ ≥2 points

Clinical and nutritional characteristics	Improved NIS burden (n=21)		Stable NIS burden (n=71)		Worsened NIS burden (n=19)	
	Baseline	Week 8	Baseline	Week 8	Baseline	Week 8
NIS burden, median (IQR)	4 (3-5)	0 (0–2)	0 (0–1)	0 (0–1)	1 (0–1)	3 (3-5)
NIS burden, n (%)						
0	0 (0)	11 (52.4)	40 (56.3)	41 (57.8)	9 (47.4)	0 (0)
1 to 2	3 (14.3)	9 (42.9)	23 (32.4)	22 (31.0)	8 (42.1)	3 (15.8)
≥ 3	18 (85.7)	1 (4.8)	8 (11.3)	8 (11.3)	2 (10.5)	16 (84.2)
Weight change (%), median (IQR)*†	−1.8 (-4.7 to 0)	−1.5 (-4.4 to 1.2)	0 (-1.3 to 0)	0 (-4.8 to 1.0)	0 (0 to 1.1)	−3.2 (-6.5 to -1.1)
Weight loss development (%), n (%)*†	–		–		–	
No weight loss	12 (57.1)	11 (52.4)	57 (82.6)	46 (64.8)	15 (83.4)	8 (42.1)
Weight gain	4 (19.0)	4 (19.1)	6 (8.7)	8 (11.3)	3 (16.7)	0 (0)
Stable weight	8 (38.1)	7 (33.3)	51 (73.9)	38 (53.5)	12 (66.7)	8 (42.1)
Weight loss	9 (42.9)	10 (47.7)	12 (17.4)	25 (35.2)	3 (16.7)	11 (57.9)
< 5%	4 (19.1)	6 (28.6)	10 (14.5)	9 (12.7)	2 (11.1)	3 (15.8)
≥ 5%	5 (23.8)	4 (19.1)	2 (2.9)	16 (22.5)	1 (5.6)	8 (42.1)
Energy intake (Kcal/kg), median (IQR)	24.3 (16.6–30.3)	29.6 (27.1–35.0)	23.6 (18.0–32.1)	26.4 (18.8–36.1)	27.4 (16.8–32.0)	21.2 (18.8–28.1)
Energy intake (Kcal/kg), n (%)						
Sufficient (≥30 Kcal/kg)	6 (28.6)	9 (42.9)	24 (33.8)	30 (42.3)	6 (31.6)	3 (15.8)

*Weight change experienced in the month before inclusion for baseline data. Weight change experienced during the 8-week follow-up W8 data.
†Missing data on baseline weight changes for three patients.

cancer and high tumour burden were more likely to improve their NIS burden. Among those with worsened NIS (42.1%), severe WL was frequent. An overall negative correlation was found between the change in NIS burden and the percentage of WL (Rho=−0.2, p=0.02).

At baseline, 75 patients (67.6%) had insufficient energy intake (median 19.9 kcal/kg) based on the 24-hour dietary recall. At W8, more patients with improved NIS burden reported stable or improved energy intake compared with those with worsened NIS burden (71.4% vs 15.8%) (table 1). They also had longer unadjusted OS (median 45.1 vs 35.9 weeks) than those with worsened NIS burden.

DISCUSSION

This study showed that changes in NIS influenced energy intake and WL in patients receiving palliative RT. We attribute the positive changes in energy and weight over 8 weeks as being related to improved symptom control since nutritional guidance was not part of the study.

One could say that this is nothing new. The relationship between NIS and WL has been explored in patients with head-and-neck cancer. These studies documented an increase in NIS burden to be associated with progressive WL. Only one assessed energy intake, but due to nutritional interventions, the link between NIS and intake was unclear.[9] Our observational study without pre-planned nutritional guidance showed that an improvement in NIS burden led to a median energy intake in line with current recommendations (30 kcal/kg),[6] but that the intake in those with worsened NIS was insufficient (21 kcal/kg). This highlights the necessity of continuous symptom monitoring, PROMs use and increased awareness of the negative impact of symptom burden on nutrition, even for patients not initially malnourished or at risk of malnutrition.

The most common NIS in this study were anorexia, feeling full and nausea, as in other studies.[4] These symptoms often go unnoticed and uncontrolled by healthcare providers.[14] PROMs were used in PRAIS for studying the effects of RT on pain with appropriate interventions initiated as necessary. The regular use of PROMs can enhance symptom awareness, improve communication about patient issues and promote individualised health practices with better outcomes.[7 8]

Some NIS are included in commonly used PROMs or should be added, if not present, to improve care and follow-up to boost energy intake and decrease WL.

The main strength of this first prospective study to evaluate the association between NIS and energy intake in advanced cancer patients is the utilisation of recognised methods (PG-SGA and GLIM) for screening and malnutrition assessment. Critics may argue that the 24-hour food recall method is limited to 1 day and does not reflect a typical nutritional intake. However, this method has proven valid for group-level energy intake assessment.[15] Multivariable statistical analysis for deeper insights was restricted due to the exclusion of 38% of patients due to missing data or death, a common problem in patients with advanced

disease. An effect of RT on nutritional status cannot be excluded but is unlikely since RT was administered for palliative purposes and limited to bone metastases. Although this was a single-centre study with some diagnoses underrepresented, findings regarding the effect of NIS on nutrition seem consistent with studies performed in other clinical settings.

Future research should assess the effects of NIS improvement on malnutrition and survival. New strategies are needed to ensure systematic assessment of nutrition and PROMs in cancer patients. MyPath (https://mypath-cancercare.eu/), a study developing digital PROMs assessments with patient-centred care pathways, could facilitate use.

CONCLUSION

This study demonstrates that changes in NIS burden directly affect energy intake and WL in a real-life cohort of patients with advanced cancer. Considering the negative impact of WL on QoL and survival, NIS should be systematically assessed and addressed.

Contributors AB and MJH were involved in planning the study, analysed and interpreted the data and were major contributors in the writing process. AU analysed and interpreted the data and was a major contributor in the writing process. EB and HS collected the data. ODs, IR and AP were involved in data analysis and interpretation and contributed towards the writing process. SK, NA and PK were involved in the planning of the study and contributed towards the writing process. All authors reviewed and approved the final article.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Regional Committee for Medical and Health Research Ethics, Central Norway (2013/1126/REK Middle Norway). Participants gave informed consent to participate in the study.

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