

This is the published version of a paper published in *Nutrition and Cancer*.

Citation for the original published paper (version of record):

Einarsson, S., Laurell, G., Tiblom Ehrsson, Y. (2020) An explorative study on energy balance in patients with head and neck cancer *Nutrition and Cancer*, 72(7): 1191-1199 https://doi.org/10.1080/01635581.2019.1676454

Access to the published version may require subscription.

N.B. When citing this work, cite the original published paper.

Permanent link to this version:

http://urn.kb.se/resolve?urn=urn:nbn:se:umu:diva-164019



Nutrition and Cancer



ISSN: 0163-5581 (Print) 1532-7914 (Online) Journal homepage: https://www.tandfonline.com/loi/hnuc20

An explorative study on energy balance in patients with head and neck cancer

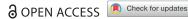
Sandra Einarsson, Göran Laurell & Ylva Tiblom Ehrsson

To cite this article: Sandra Einarsson, Göran Laurell & Ylva Tiblom Ehrsson (2020) An explorative study on energy balance in patients with head and neck cancer, Nutrition and Cancer, 72:7, 1191-1199, DOI: 10.1080/01635581.2019.1676454

To link to this article: https://doi.org/10.1080/01635581.2019.1676454

9	© 2019 The Author(s). Published with license by Taylor & Francis Group, LLC.					
	Published online: 12 Oct 2019.					
	Submit your article to this journal 🗷					
hil	Article views: 1119					
α	View related articles 🗹					
CrossMark	View Crossmark data ☑					







An explorative study on energy balance in patients with head and neck cancer

Sandra Einarsson^a (D), Göran Laurell^b (D), and Ylva Tiblom Ehrsson^b (D)

^aDepartment of Food and Nutrition, Umeå University, Umeå, Sweden; ^bDepartment of Surgical Sciences, Section of Otorhinolaryngology and Head & Neck Surgery, Uppsala University, Uppsala, Sweden

ABSTRACT

Background: Involuntary body weight loss in head and neck cancer is common. Fundamental for weight loss is an energy imbalance where total energy expenditure exceeds energy intake. Aim: To map energy intake and parameters of energy expenditure at the start of and after radiotherapy, and their relation to weight change, body mass index, and immune markers in patients with head and neck cancer.

Materials and Methods: Data from 20 patients on energy intake (24-hour dietary intake recalls), total energy expenditure (SenseWear Armband Pro3), resting energy expenditure (indirect calorimetry), body weight, body mass index, and immune markers in serum (C-reactive protein and Interleukin-6) were collected at the start of and after radiotherapy (median 8 mo, range 5-13).

Results: No statistical significance was shown between the two measurement points for energy intake or for the different parameters of energy expenditure. Median values for energy balance were 0.93 and 0.96 for the start of treatment and follow-up, respectively. Twelve and 13 patients had a negative energy balance at the start of radiotherapy and at follow-up, respectively.

Conclusion: A negative energy balance was seen for the majority of patients, which stresses the importance of nutritional treatment at the start of and after radiotherapy.

ARTICLE HISTORY

Received 8 May 2019 Accepted 27 September 2019

Introduction

Patients with head and neck cancer (HNC) often experience significant body weight loss during and after treatment (1-3). Fundamental for this weight loss is an energy imbalance where total energy expenditure exceeds energy intake (4).

There are many factors affecting energy intake in patients with HNC. Tumor site might cause insufficient food intake due to mechanical obstruction or pain (5), and treatment, i.e., radiotherapy (RT), surgery, and/or anticancer drugs might cause toxicities that affect food intake both during and after treatment (6,7).

The primary components of energy expenditure are basal energy expenditure and physical activity, both of which can be altered in patients with cancer (4). Reduced energy expenditure might be the result of reduced physical activity because of reduced physical function (8) and fatigue (9). Basal energy expenditure can be elevated, normal, or reduced (10,11), and this response might vary

among different cancer types (12) as well as among individuals (13). More specifically, the inflammatory and metabolic response due to a tumor and/or treatment might increase basal energy expenditure (4,14,15).

Weight loss is a central criterion for diagnosing patients for malnutrition (16). Reduced fat-free mass has been correlated in studies on HNC to reduced hand grip strength (17) and impaired physical performance (8,17). Involuntary weight loss has important clinical implications because it is related to the development of malnutrition-related complications. Thus, for the surveillance of patients with HNC it would be useful to establish more knowledge on the relation between weight loss, body mass index (BMI), and energy balance.

Aim

The aim of the present study was to map energy intake and different parameters of energy expenditure at the start of and after radiotherapy and their relation

Table 1. Patient characteristics (n = 20).

Patient no.	Tumor location	TNM classification	Stage ^a	Treatment modality ^b
1	Tonsil	T2N2bM0	IVA	CF, neck dissection
2	Tongue	T2N1M0	III	AF, hemiglossectomy + neck dissection
3	Other oropharynx	T1N2bM0	IVA	CF, neck dissection
4	Tonsil	T2N2M0	IVA	CF, neck dissection
5	Tonsil	T1N3M0	IVB	CF
6	Unknown primary	T0N2aM0	_	CF
7	Tonsil	T1N2bM0	IVA	CF
8	Tonsil	T2N2bM0	IVA	CF
9	Tonsil	T1N2bM0	IVA	CF, neck dissection
10	Tonsil	T2N0M0	II	CF
11	Tonsil	T1N2bM0	IVA	CF
12	Base of tongue	T1N2bM0	IVA	CF, neck dissection
13	Base of tongue	T1N0M0	1	CF
14	Tonsil	T1N2cM0	IVA	CF
15	Base of tongue	T3N2bM0	IVA	CF, neck dissection
16	Tonsil	T3N0M0	III	CF
17	Tonsil	T2N2bM0	IVA	CF, neck dissection
18	Unknown primary	T0N1M0	_	Neck dissection, CF
19	Base of tongue	T3N1M0	III	CF, neck dissection
20	Tongue	T2N0M0	II	AF, hemiglossectomy

^aUICC version 7.

to weight change, body mass index, and immune markers in patients with head and neck cancer.

Materials and methods

From 2010 to 2013, 20 patients were recruited from a tertiary care hospital in Sweden. Patients ≥18 years of age with a newly diagnosed HNC planned for curative RT were eligible and were consecutively asked to participate in the study by a research nurse. Exclusion criteria were dementia, physiological illness, or a social situation that would affect the possibility for the patient to complete the study. The patients received either RT (conventional fractionation or accelerated fractionation) as a single modality treatment or RT followed by surgery. Treatment details for each patient are shown in Table 1. Nutritional treatment according to the hospital regimes was given with the intent of keeping the patient in a steady energy state. None of the patients had tube feeding or parenteral nutrition at any of the measurement points.

Study subjects

All patients in the study cohort were men, and the median age was 54.5 years (range 43-71 years). Detailed tumor characteristics for each patient are shown in Table 1 (16 oropharyngeal, two oral cavity, and two unknown primary).

Data collection

Patients were measured at the start of RT (before the start or during the first week of RT) and with a median follow-up of 8 mo, (range 5-13 mo). The

follow-up was chosen to capture the effect of late treatment toxicities rather than acute and occurred in a time when patients returned to the hospital for a medical checkup. One patient (no. 5) did not complete the second measurements because of a palliative situation. At both occasions, data on energy intake, energy expenditure, anthropometric measures, and immune markers were gathered.

Measures of energy intake

Data for energy intake were collected during two weekdays and one weekend (only on weekdays for n = 2) using 24-hour dietary intake recalls. First, patients gave written information on the food and beverages consumed. Second, a dietitian gathered detailed information about food selection and portion sizes through a face-to-face (first measurement) or a telephone (second measurement) interview. Portion sizes were estimated using household measures and pictures for different portion sizes and food types from the Swedish National Food Administration (18). These were sent to the patients' home before the telephone interview. Energy intake for each day was estimated using the software program Dietist XP version 3.2 (Kost och Näringsdata AB), and the mean value was used in the analyses.

Measures of energy expenditure

Total energy expenditure was collected using a device called the SenseWear Armband Pro3 (SWA, BodyMedia, Inc., Pittsburgh, PA, USA) (19). The armband is worn on the upper part of the right arm and uses sensors to

^bType of surgery and radiotherapy are specified. CF: Conventional fractionation (2.0 Gy/day, total 68 Gy over 7 weeks), AF: Accelerated fractionation (1.1 Gy + 2.0 Gy/day, total 68 Gy over 4.5 weeks).

measure movement, heat flux, skin temperature, near body temperature, and galvanic skin response. The software program Interview Professional (version 6.1) estimates total energy expenditure from the SWA together with information about the patient's age, sex, height, weight, and whether the patient is a smoker or nonsmoker and is right or left handed. Patients used the SWA during the same three days as the self-reported 24h dietary intake recalls, and the mean value was used in the analyses. For six patients, data from the SWA were available for two days, and for one patient the total energy expenditure and energy intake were not measured on the same days. The armband was taken off during RT or to avoid coming in contact with water. During this time, the software program calculated an estimation of energy expenditure corresponding to the patients' basal energy expenditure. Only days in which the armband was worn at least 20 h, were used in the analyses (missing, n = 4 days).

Energy balance was calculated as the energy intake divided by the total energy expenditure. For values >1, patients were presumed to be in positive energy balance, whereas for values <1 the patients were presumed to be in negative energy balance.

Resting energy expenditure was measured by indirect calorimetry (DeltratracTM II MBM 200). Patients had fasted for four hours, and the measurements took place over 30 mins, with the patient in a supine position (20). Physical activity level was calculated by subtracting the resting energy expenditure from the total energy expenditure.

Anthropometric measures

Height and weight were measured using a wall stadiometer (to the nearest 0.1 cm) and an electronic scale (to the nearest 0.1 kg). The patients wore light clothing and no shoes for the measurements. Weights at start of RT and at follow-up were used to calculate relative percentage weight loss. Weight loss of 5-10% was classified as moderate and weight loss of >10% was classified as severe (16), and a third group consisted of patients with weight gain, no change in weight, or little weight loss (<5%). Patients were also divided into groups based on their BMI (weight in kilograms divided by height in meters squared) as underweight (BMI <20), normal weight (BMI 20-25), and overweight or obese (BMI >25) (16). For patients over 70 years, BMI <22 was considered underweight and BMI between 22 and 27 was considered normal. Malnutrition was defined using the Global Leadership Initiative on Malnutrition (GLIM) criteria (16), which

is a consensus from the global clinical nutrition community on how to diagnose malnutrition. For the diagnosis of malnutrition, at least one phenotypic criterion and one etiologic criterion should be present, i.e., weight loss, low BMI, or reduced fat-free mass (phenotypic factors) and reduced food intake or inflammation (etiologic factors).

Blood samples

Blood samples (four-hour fasting values) were gathered for analyses of the immune markers C-reactive protein (CRP, ref <10 mg/L) and Interleukin-6 (IL-6, ref <7 ng/L).

Ethical approval

The Regional Ethical Review Board in Umeå, Sweden (Dnr 2010-24-31), approved the study, and all patients signed written informed consent forms.

Statistical analyses

Non-parametric tests were used due to the limited number of patients. For these statistical analyses, the data software Statistical Package for the Social Sciences (SPSS) version 25.0 was used. The Wilcoxon signed rank test was used to analyze the change in weight, BMI, total energy expenditure, resting energy expenditure, energy intake, and physical activity level between the two measured points. The Mann-Whitney U-test was used to analyze total energy expenditure in patients with CRP and/or IL-6 above reference values compared to patients with CRP and IL-6 in the normal range. The correlation between energy balance and weight change percent or BMI was carried out using the Spearman rank test. All tests were two-sided, and a p-value ≤ 0.05 was considered statistically significant.

Results

Energy intake and energy expenditure

Data for energy intake and energy expenditure at start and follow-up are shown in Table 2, and relative change in percent is shown in Figure 1. No statistical significance was seen between the start of RT and follow-up for any of the variables: energy intake (z =-0.806, N - Ties = 18, p = 0.420), total energy expenditure (z = -0.501, N - Ties = 18, p = 0.616), resting energy expenditure (z = -1.605, N - Ties = 17, p = 0.109) and energy spent on physical activity (z

Table 2. Energy intake and energy expenditure at the start of radiotherapy and at follow-up (median 8 mo, range 5-13 mo,) in the study cohort (n = 20).

Patient no.	Total energy expenditure (kcal/24 h) ^a		Resting energy expenditure (kcal/24 h) ^b		Energy intake (kcal/24 h) ^c		Physical activity (kcal/24 h) ^d	
	Start	Follow-up	Start	Follow-up	Start	Follow-up	Start	Follow-up
1	2485.50	2097.67	1760	1650	2471.67	3437.67	725.50	447.67
2	2655.50	2802.00	1790	_	1811.33	1240.67	865.50	_
3	3016.00	2757.00	1690	1550	2556.33	2614.67	1326.00	1207.00
4	2207.00	2216.00	1410	1330	2346.33	2152.67	797.00	886.00
5	2256.67	_	1600	_	1526.00	_	656.67	_
6	2801.00	2864.67	1770	1770	4507.67	3545.00	1031.00	1094.67
7	2843.00	3036.00	1680	1650	2646.00	2005.00	1163.00	1386.00
8	2448.33	2797.00	1650	1880	2793.67	3224.67	798.33	917.00
9	3013.67	3097.00	1670	1560	2168.67	2456.33	1343.67	1537.00
10	2028.67	2516.33	1290	1250	2073.67	1884.67	738.67	1266.33
11	3110.67	2646.67	1730	1580	3197.00	2595.33	1380.67	1066.67
12	2776.00	2522.67	1760	1380	2856.33	2647.33	1016.00	1142.67
13	3634.67	3390.00	1670	1730	2801.00	3322.00	1964.67	1660.00
14	2339.33	1975.33	1850	1690	2178.67	2729.00	489.33	285.33
15	2623.33	2773.00	1940	1910	1806.33	1728.00	683.33	863.00
16	3110.00	3401.00	1820	1620	2320.00	2232.00	1290.00	1781.00
17	2611.33	3569.00	1780	1920	1695.33	1895.67	831.33	1649.00
18	2214.00	2188.67	1500	1290	2454.33	2187.33	714.00	898.67
19	2741.33	3099.67	1800	_	3804.00	2865.00	941.33	_
20	2112.00	_	1500	1640	1703.67	-	612.00	_
Median	2639.42	2785.00	1710.00	1640.00	2400.33	2525.83	848.42	1118.67
(Q_1, Q_3)	(2277.33,	(2441.25,	(1612.50,	(1465.00,	(1876.92,	(1977.67,	(716.88,	(889.17,
	2971.00)	3097.67)	1787.50)	1750.00)	2799.17)	2954.92)	1258.25)	1499.25)

 $[\]overline{^{a}}$ Wilcoxon's test, p = 0.616.

^dWilcoxon's test, p = 0.326.

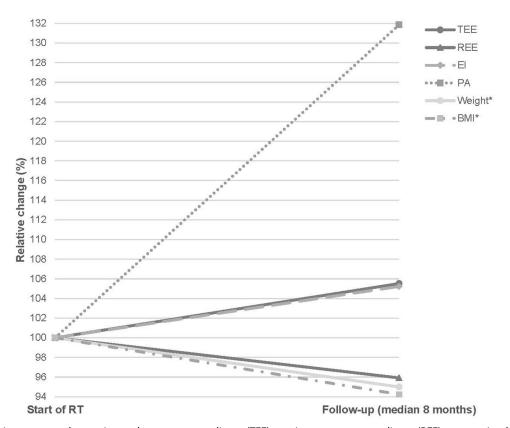


Figure 1. Relative percent change in total energy expenditure (TEE), resting energy expenditure (REE), energy intake (EI), physical activity (PA), weight, and body mass index (BMI) in patients with head and neck cancer from the start of radiotherapy (RT) to follow-up (median 8 mo, range 5–13 mo). *Wilcoxon's test, p < 0.001.

^bWilcoxon's test, p = 0.109.

^cWilcoxon's test, p = 0.420.

= -0.982, N - Ties = 16, p = 0.326). At follow-up, eleven patients had increased and five patients had decreased their energy spent on physical activity (missing, n = 4).

Median values for total energy expenditure recalculated to kcal per kilo body weight per day were 32.0 (Q₁ 28.8, Q₃ 33.5) at the start of RT and 34.5 $(Q_1 30.9, Q_3 40.5)$ at follow-up. Median values for energy balance, i.e., energy intake divided by total energy expenditure were 0.93 (Q₁ 0.73, Q₃ 1.05) and 0.96 (Q₁ 0.66, Q₃ 1.08) for the start of treatment and follow-up, respectively. Twelve patients had a negative energy balance, i.e., their values for energy intake were lower than the total energy expenditure at the start of RT (median -760 kcal, Q₁ -842 kcal, Q₃ -250 kcal), and eight patients had a positive energy balance (median 190 kcal, Q1 82 kcal, Q3 883 kcal), i.e., their values for energy intake were higher than the total energy expenditure at the start of RT. At followup, 13 patients had a negative energy balance (median $-632\,kcal,~Q_1~-1107\,kcal,~Q_3~-66\,kcal)$ and five patients had a positive energy balance (median 680 kcal, Q_1 276 kcal, Q_3 1047 kcal) (missing, n = 2).

Nutritional status

One patient was diagnosed as malnourished at the start of RT (no. 20), and the corresponding number at follow-up was three patients (no. 2, 13, 16). Relative change in percent for weight and BMI is shown in Figure 1. Weight changed significantly between the two measurements (z = -3.784, N - Ties = 19, p < 0.001). Median weights at the start of RT and at follow-up were 85.8 kg (Q₁ 78.0, Q₃ 90.7) and 81.5 (Q₁ 71.8, Q₃ 83.1), respectively, corresponding to a percentage weight loss of -8.1% (Q₁ -11.6, Q₃ -4.5). Six patients had severe weight loss (>10%), eight patients a moderate weight loss (5-10%), four had little weight loss (< 5%), and one patient gained weight (missing, n = 1). There was no correlation between weight change percent and energy balance assessed at the start of RT (r = -0.109, N = 19, p = 0.658) or at follow-up (r = -0.228, N = 18, p = 0.363).

There was a significant decrease in BMI between the two measurements (z = -3.783, N - Ties = 19, p < 0.001). Median BMI at the start of RT and at follow-up were 26.0 (Q₁ 24.2, Q₃ 27.3) and 24.5 (min 22.6, max 26.0), respectively. At the start of RT, one patient was underweight, five patients were normal weight, and 14 patients were overweight/obese. At follow-up, two patients were underweight, eleven patients were normal weight, and six patients were

Table 3. Immune markers at the start of radiotherapy and at follow-up (median 8 mo, range 5-13 mo,) in the study cohort (n = 20).

		tive protein e <10 mg/L) ^a		Interleukin-6 (reference <7 ng/L) ^b		
Patient no.	Start	Start Follow-up		Follow-up		
1	<5	<5	3	_		
2	8	6	4	10		
3	21	<5	11	2		
4	<5	<5	2	5		
5	135	_	76	_		
6	_	<5	2	2		
7	<5	<5	2	3		
8	<5	<5	5	3		
9	<5	<5	2	4		
10	10	<5	4	3		
11	<5	<5	4	5		
12	<5	<5	3	2		
13	<5	<5	43	74		
14	<5	7	4	6		
15	14	<5	6	2		
16	<5	15	5	2		
17	<5	<5	2	3		
18	<5	_	2	_		
19	<5	<5	2	3		
20	<5	<5	2	5		

^aWilcoxon's test, p = 0.400. ^bWilcoxon's test, p = 0.466.

overweight/obese. There was no correlation between BMI and energy balance at the start of RT (r = -0.011, N = 20, p = 0.965) or at the follow-up (r = -0.0.051, N = 18, p = 0.842), respectively.

Immune markers

Data for immune markers are presented in Table 3. Median values for CRP were 5.0 mg/L (Q₁ 5.0, Q₃ 8.0) and 5.0 mg/L (Q₁ 5.0, Q₃ 5.0) at the start of RT and at follow-up, respectively. The corresponding values for IL-6 were 3.5 ng/L (Q₁ 2.0, Q₃ 5.0) and 3.0 ng/L $(Q_1 2.0, Q_3 5.0)$, respectively. At the start of RT, five patients had elevated CRP and/or IL-6 above reference values. These patients had a significantly higher $(U = 11, N_1 = 5, N_2 = 14, p = 0.026)$ total energy expenditure at the start of RT (33.7 kcal/kg body weight/day, Q₁ 31.4, Q₃ 39.3) compared to patients with CRP and IL-6 in the normal range (median 29.9 kcal/kg body weight/day, Q₁ 28.4, Q₃ 33.1). At follow-up three patients had elevated levels of CRP and IL-6, but a significant increase in energy expenditure could not be found for these patients (U = 13, $N_1 = 3$, $N_2 = 14$, p = 0.313).

Discussion

The present study was undertaken to map the energy balance in patients with HNC at the start of and after RT. No statistical significance was shown between the

start of RT and follow-up for energy intake or for any parameters of energy expenditure.

Previous studies on energy intake in patients with HNC have shown a decrease in energy intake during RT and a subsequent increase during revalidation. Kenway et al. (21) and van den Berg et al. (22) studied energy intake in patients with nasopharyngeal cancer (n = 38) and patients with different tumors of the head and neck (n=47) and found a decrease in energy intake during RT with a significant increase in energy intake at two months and six months post RT. In studies by Jager-Wittenaar et al. (17) and Silver et al. (8) on patients with different tumors of the head and neck (n = 29 and n = 17, respectively), no significant differences were found for energy intake over time (from the start of RT up to one and four months post RT). Additionally, the study by Kenway et al. (21) did not show significant differences in energy intake between the start of RT and revalidation at two and six months post RT. The current study adds important information to previous studies because it presents results on energy intake over a longer perspective after the termination of treatment. No significant difference in energy intake was shown between the start of RT and follow-up, and therefore the results from the present and previous studies indicate that patients with HNC in general can recover their energy intake and return to pre-RT energy intake in a long-term perspective after the termination of RT. However, how well this intake corresponds to the energy expenditure has not been previously well documented in HNC.

Though not significant, the relative change in percent for resting energy expenditure decreased from the start of RT to follow-up. Compared to the situation at the start of RT, previous studies have shown a significant decrease in resting energy expenditure during treatment (23) and up to three (24) and six months (21) after RT. Again, the present study adds important information on energy expenditure in HNC and implies lower values for resting energy expenditure after RT, probably due to reduced body weight (21). The current study also showed that the energy spent on physical activity increased from the start of RT to follow-up, which might be explained by improved physical function at the follow-up. The net effect for the decrease in resting energy expenditure and the increase in physical activity seen in this study was a relatively steady state on the group level in terms of total energy expenditure between the two measurement points.

Median values for energy balance were 0.93 and 0.96 at the start of RT and at follow-up, respectively. A previous study on patients with nasopharyngeal cancer showed data on total energy expenditure at the start of RT, end of RT, and at two and six months post RT by adding the resting energy expenditure measured by indirect calorimetry to energy spent on physical activity estimated by questionnaires (21). That study found a negative energy balance through all time points, with the largest difference between energy intake and energy expenditure at the start and end of RT. In the present study, twelve patients had a negative energy balance at the start of RT, corresponding to a median energy deficit of 760 kcal. The corresponding number at follow-up was 13 patients with a median energy deficit of 632 kcal. It is well known that patients with HNC might struggle with long-term treatment sequelae (7) that have an impact on many aspects related to food and eating (25). Xerostomia and mucosal sensitivity have, for example, been shown to significantly impact energy intake after RT (26). Along with the result from the present study, imposing a negative energy balance for the majority of patients both at the start of RT and at follow-up stresses the importance of nutritional treatment at the start of RT as well as for HNC patients who suffer from long-term treatment toxicities.

Weight and BMI deteriorated significantly during the study period, which is in line with reports from earlier studies on patients with HNC (1-3). The largest weight loss has previously been seen during RT with a nadir at six months after the termination of treatment (1,3). The present study could not establish a direct correlation between weight change or BMI and energy balance, which previously has been described to be due to the fact that recovery in weight lags behind recovery in energy intake (21). Earlier studies on HNC have shown that 60-70% of the body weight loss is loss of fat-free mass (8,17). In the present study, only one patient at the start of RT and three patients at follow-up were malnourished according to the GLIM criteria (16). In these new criteria, at least one phenotypic criterion and one etiologic criterion should be present for the diagnosis of malnutrition, i.e., weight loss, low BMI, or reduced fat-free mass (phenotypic factors) and reduced food intake or inflammation (etiologic factors). Many of the patients in the present study had one etiologic factor (mainly reduced food intake), but few had a phenotypic factor despite the high prevalence of weight loss since few patients had a weight loss of >10% beyond six months. This indicates the importance of having

information on fat-free mass in order to be able to decipher the patients' nutritional status further. Also, because fat-free mass is closely related to resting energy expenditure (24), assessment of fat-free mass would have added valuable information to the present study, enabling a more in-depth interpretation of the relationship between nutritional status and energy balance in HNC.

The present study also showed that patients with elevated immune markers, i.e., CRP and/or IL-6 above reference at the start of RT, had a significantly higher total energy expenditure compared to patients with values in the normal range. The contribution of disease-related inflammation to the development of malnutrition is reported to be the increase of resting energy expenditure and muscle catabolism (16), and cancer diseases have in general been stated to be associated with recurrent or chronic inflammation (15,16). Moreover, systemic inflammation might be induced in response to RT (14). To decipher if patients with HNC who present with elevated immune markers can be regarded as a risk group for malnutrition would therefore be an interesting approach for future studies.

The level of evidence for energy requirements in patients with cancer is low because few studies have measured total energy expenditure in patients with cancer, and all studies performed to date have all had small study samples (27-32). Existing guidelines on energy requirements for patients with cancer have been set to 25-30 kcal/kg body weight/day (33). From a clinical perspective, treatment centers in Sweden often use 30-35 kcal/kg body weight/day when calculating energy requirements in patients with HNC. A previous study on patients with HNC showed a loss of body weight and fat-free mass after RT with intakes <35 kcal/kg/day (17). The results from the present study showed that median values for total energy expenditure were 32.0 kcal/kg body weight/day at the start of RT and 34.5 kcal/kg body weight/day at follow-up. Hence, existing guidelines on energy requirements for patients with cancer might be correct on a group level at the start of RT but likely underestimate energy requirements after RT in patients with HNC. The results from the present study were generated from male patients exclusively. Women might have a lower energy expenditure than men, which can mainly be explained by differences in body composition between men and women (34), and this should be taken into account when considering how the results from the present study might be applied in clinical practice.

To our knowledge, only three previous studies have used SWA to measure energy expenditure in patients with malignant disorders, i.e., studies on acute myelogenous leukemia (n = 10 patients) (30), gastrointestinal cancer (n = 14 patients) (31), and gastrointestinal cancer (n = 6 patients) (32), thus making the present study the first to use SWA in patients with HNC. SWA measures have been shown to correlate well with energy expenditure in healthy individuals with low moderate physical activity (19,35).Additionally, a small pilot study on patients with malignant disorders has also showed promising validity (30). In a study by Viggiani et al. (32), patients with gastrointestinal cancer received nutritional counseling according to their measured total energy expenditure, and because the patients remained weight stable throughout the course of treatment, the authors concluded that nutritional treatment could be based on SWA measurements. However, studies are needed to further establish the accuracy of the SWA armband in a clinical setting.

The present study includes data from a rather small number of patients, and the results should therefore be interpreted as hypothesis generating. Selection bias should also be considered because patients who accepted participation might be in a better disease and nutritional state than patients who refrained. One important strength of this study is the extensive data collection for each patient. The measure of total energy expenditure has only been measured in few earlier studies on patients with cancer (27-32). It is difficult to capture true day-to-day variation when collecting data on total energy expenditure and energy intake and the data from the present study consist of mean values from three subsequent days at the start of treatment and follow-up. Dietary intake methods have limitations of patient memory and that the results rest on what the patients want to convey about their eating.

In conclusion, the present study adds important knowledge about nutritional surveillance in patients with HNC because few studies have mapped energy intake and different parameters of energy expenditure in patients with cancer, especially including information on total energy expenditure. A negative energy balance was seen for the majority of patients both at the start of RT and at follow-up, which stresses the importance of nutritional treatment for patients with HNC both at the start of RT and for the patients who suffer from long-term treatment toxicities. Also, current recommendations on energy requirements in patients with cancer likely underestimate energy expenditure on the group level in HNC after RT,

however larger studies on a heterogeneous patient cohort need to be conducted to establish the applicability in clinical practice.

Disclosure statement

The authors report no conflict of interest.

Funding

This work was supported by ALF grants from Umeå University Hospital; The Swedish Cancer Society under Grant number CAN 2008/772 and number CAN 2015/363; The Kamprad Family Foundation for Entrepreneurship, Research & Charity under Grant number 20150003. Thanks to research nurse Inger Arnesjö, specialist nurse Brith Granström, and the participating patients.

ORCID

Sandra Einarsson (b) http://orcid.org/0000-0003-4770-3726 Göran Laurell (b) http://orcid.org/0000-0002-7760-246X Ylva Tiblom Ehrsson (b) http://orcid.org/0000-0001-7435-167X

References

- 1. Ottosson S, Zackrisson B, Kjellén E, Nilsson P, Laurell G. Weight loss in patients with head and neck cancer during and after conventional and accelerated radiotherapy. Acta Oncol. 2013;52(4):711–718.
- 2. Newman LA, Vieira F, Schwiezer V, Samant S, Murry T, Woodson G, Kumar P, Robbins KT. Eating and weight changes following chemoradiation therapy for advanced head and neck cancer. Arch Otolaryngol Head Neck Surg. 1998;124(5):589–592.
- 3. Ehrsson YT, Langius-Eklöf A, Laurell G. Nutritional surveillance and weight loss in head and neck cancer patients. Support Care Cancer. 2012;20(4):757–765.
- 4. Purcell SA, Elliott SA, Baracos VE, Chu QSC, Prado CM. Key determinants of energy expenditure in cancer and implications for clinical practice. Eur J Clin Nutr. 2016;70(11):1230–1238.
- 5. List MA, Bilir SP. Functional outcomes in head and neck cancer. Semin Radiat Oncol. 2004;14(2):178–189.
- 6. Chasen MR, Bhargava R. A descriptive review of the factors contributing to nutritional compromise in patients with head and neck cancer. Support Care Cancer. 2009;17(11):1345–1351.
- Trotti A. Toxicity in head and neck cancer: a review of trends and issues. Int J Radiat Oncol Biol Phys. 2000;47(1):1–12.
- 8. Silver HJ, Dietrich MS, Murphy BA. Changes in body mass, energy balance, physical function, and inflammatory state in patients with locally advanced head and neck cancer treated with concurrent chemoradiation after low-dose induction chemotherapy. Head Neck. 2007;29(10):893–900.

- 9. Jereczek-Fossa BA, Marsiglia HR, Orecchia R. Radiotherapy-related fatigue. Crit Rev Oncol Hematol. 2002;41(3):317–325.
- Bosaeus I, Daneryd P, Svanberg E, Lundholm K. Dietary intake and resting energy expenditure in relation to weight loss in unselected cancer patients. Int J Cancer. 2001;93(3):380–383.
- 11. Cao D-X, Wu G-h, Zhang B, Quan Y-J, Wei J, Jin H, Jiang Y, Yang Z-A. Resting energy expenditure and body composition in patients with newly detected cancer. Clin Nutr. 2010;29(1):72–77.
- 12. Fredrix EWHM, Soeters PB, Wouters EFM, Deerenberg IM, von Meyenfeldt MF, Saris WHM. Energy balance in relation to cancer cachexia. Clin Nutr. 1990;9(6):319–324.
- 13. Fredrix EWHM, Wouters EFM, Soeters PB, Van Der Aalst ACJM, Kester ADM, Von Meyenfeldt MF, Saris WHM. Resting energy expenditure in patients with non-small cell lung cancer. Cancer. 1991;68(7): 1616–1621.
- 14. Schaue D, Micewicz ED, Ratikan JA, Xie MW, Cheng G, McBride WH. Radiation and inflammation. Semin Radiat Oncol. 2015;25(1):4–10.
- 15. Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. Lancet Oncol. 2014;15(11):e493–e503.
- 16. Cederholm T, Jensen G, Correia M, Gonzalez M, Fukushima R, et al. GLIM criteria for the diagnosis of malnutrition—A consensus report from the global clinical nutrition community. J Cachexia Sarcopenia Muscle. 2019;10:201–217.
- 17. Jager Wittenaar H, Dijkstra P, Vissink A, Langendijk J, van der Laan B, et al. Changes in nutritional status and dietary intake during and after head and neck cancer treatment. Head Neck. 2011;33:863–870.
- 18. Swedish National Food Administration [Internet]. Sweden: Swedish National Food Administration; 2009 [cited 2019 Jan 14]. Available from: https://www.livs-medelsverket.se/globalassets/publikationsdatabas/bro-schyrer/portionsguiden.pdf.
- 19. St-Onge M, Mignault D, Allison DB, Rabasa-Lhoret R. Evaluation of a portable device to measure daily energy expenditure in free-living adults. Am J Clin Nutr. 2007;85(3):742–749.
- Compher C, Frankenfield D, Keim N, Roth-Yousey L. Best practice methods to apply to measurement of resting metabolic rate in adults: a systematic review. J Am Diet Assoc. 2006;106(6):881–903.
- 21. Ng K, Leung SF, Johnson PJ, Woo J. Nutritional consequences of radiotherapy in nasopharynx cancer patients. Nutr Cancer. 2004;49(2):156–161.
- 22. van den Berg MGA, Rasmussen-Conrad EL, Gwasara GM, Krabbe PFM, Naber AHJ, Merkx MA. A prospective study on weight loss and energy intake in patients with head and neck cancer, during diagnosis, treatment and revalidation. Clin Nutr. 2006;25(5): 765–772.
- 23. García-Peris P, Lozano MA, Velasco C, de La Cuerda C, Iriondo T, Bretón I, Camblor M, Navarro C. Prospective study of resting energy expenditure changes in head and neck cancer patients treated with

- chemoradiotherapy measured by indirect calorimetry. Nutrition. 2005;21(11-12):1107-1112.
- Langius JAE, Kruizenga HM, Uitdehaag BMJ, Langendijk JA, Doornaert P, Leemans CR, Weijs PJM. Resting energy expenditure in head and neck cancer patients before and during radiotherapy. Clin Nutr. 2012;31(4):549–554.
- 25. Einarsson S, Laurell G, Tiblom Ehrsson Y. Experiences and coping strategies related to food and eating up to two years after the termination of treatment in patients with head and neck cancer. Eur J Cancer Care. 2019;28(2):e12964.
- Ganzer H, Touger-Decker R, Parrott JS, Murphy BA, 26. Epstein JB, Huhmann MB. Symptom burden in head and neck cancer: impact upon oral energy and protein intake. Support Care Cancer. 2013;21(2):495-503.
- Gibney E, Elia M, Jebb S, Murgatroyd P, Jennings G. Total energy expenditure in patients with small-cell lung cancer: results of a validated study using the bicarbonate-urea method. Metabolism. 1997;46(12): 1412-1417.
- Demark-Wahnefried W, Hars V, Conaway MR, Havlin K, Rimer BK, McElveen G, Winer EP. Reduced rates of metabolism and decreased physical activity in breast cancer patients receiving adjuvant chemotherapy. Am J Clin Nutr. 1997;65(5):1495–1501.
- Moses A, Slater C, Preston T, Barber M, Fearon K. Reduced total energy expenditure and physical activity

- in cachectic patients with pancreatic cancer can be modulated by an energy and protein dense oral supplement enriched with n-3 fatty acids. Br J Cancer. 2004;90(5):996-1202.
- 30. Cereda E, Turrini M, Ciapanna D, Marbello L, Pietrobelli A, Corradi E. Assessing energy expenditure in cancer patients: a pilot validation of a new wearable device. JPEN J Parenter Enteral Nutr. 2007;31(6):
- Bencini L, Di Leo A, Pozzessere D, Bozzetti F. Total 31. energy expenditure in patients with advanced solid tumors: a preliminary report. Nutr Ther Metab. 2008; 26:45-47.
- 32. Viggiani MT, Lorusso O, Natalizio F, Principi M, Di Leo A, Barone M. Influence of chemotherapy on total energy expenditure in patients with gastrointestinal cancer: a pilot study. Nutrition. 2017;42:7-11.
- Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, Fearon K, Hütterer E, Isenring E, Kaasa S, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017;36(1):11-48.
- 34. Westerterp KR. Control of energy expenditure in humans. Eur J Clin Nutr. 2017;71(3):340-344.
- Koehler K, Drenowatz C. Monitoring energy expend-35. iture using a multi-sensor device-applications and limitations of the SenseWear armband in athletic populations. Front Physiol. 2017;8:983