Nutrition and Cancer

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/hnuc20

Effect of Early Individualized Dietary Counseling on Weight Loss, Complications, and Length of Hospital Stay in Patients With Head and Neck Cancer: A Comparative Study

Eva Leistra[ab], Simone E. J. Eerenstein[c], Loes H. van Aken[a], Femke Jansen[c], Marian A. E. de van der Schueren[ad], Jos W. R. Twisk[e], Marjolein Visser[ef] & Jacqueline A. E. Langius[ag]

[a] Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands

[b] Department of Nutrition and Dietetics, School of Sports and Nutrition, Amsterdam University of Applied Sciences, Amsterdam, The Netherlands

[c] Department of Otolaryngology/Head and Neck Surgery, VU University Medical Center, Amsterdam, The Netherlands

[d] Department of Nutrition, Sports, and Health, HAN University of Applied Sciences, Nijmegen, The Netherlands

[e] Department of Epidemiology and Biostatistics, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands

[f] Department of Health Sciences, Faculty of Earth and Life Sciences, VU University, Amsterdam, The Netherlands

[g] Academy of Health, The Hague University of Applied Sciences, The Hague, The Netherlands

Published online: 28 Aug 2015.

To cite this article: Eva Leistra, Simone E. J. Eerenstein, Loes H. van Aken, Femke Jansen, Marian A. E. de van der Schueren, Jos W. R. Twisk, Marjolein Visser & Jacqueline A. E. Langius (2015): Effect of Early Individualized Dietary Counseling on Weight Loss, Complications, and Length of Hospital Stay in Patients With Head and Neck Cancer: A Comparative Study, Nutrition and Cancer, DOI: 10.1080/01635581.2015.1073755

To link to this article: http://dx.doi.org/10.1080/01635581.2015.1073755

Nutrition and Cancer, 0(0), 1–11

ISSN: 0163-5581 print / 1532-7914 online
DOI: 10.1080/01635581.2015.1073755

Routledge
Taylor & Francis Group

Effect of Early Individualized Dietary Counseling on Weight Loss, Complications, and Length of Hospital Stay in Patients With Head and Neck Cancer: A Comparative Study

Eva Leistra
Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands; Department of Nutrition and Dietetics, School of Sports and Nutrition, Amsterdam University of Applied Sciences, Amsterdam, The Netherlands

Simone E. J. Eerenstein
Department of Otolaryngology/Head and Neck Surgery, VU University Medical Center, Amsterdam, The Netherlands

Loes H. van Aken
Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands

Femke Jansen
Department of Otolaryngology/Head and Neck Surgery, VU University Medical Center, Amsterdam, The Netherlands

Marian A. E. de van der Schueren
Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands; and Department of Nutrition, Sports, and Health, HAN University of Applied Sciences, Nijmegen, The Netherlands

Jos W. R. Twisk
Department of Epidemiology and Biostatistics, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands

Marjolein Visser
Department of Epidemiology and Biostatistics, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands; and Department of Health Sciences, Faculty of Earth and Life Sciences, VU University, Amsterdam, The Netherlands

Jacqueline A. E. Langius
Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands; and Academy of Health, The Hague University of Applied Sciences, The Hague, The Netherlands

Patients with head and neck cancer (HNC) are at risk for undernutrition. Dietary counseling during treatment has positive effects on nutritional status and quality of life, however, the effects of dietary counseling started before initiation of treatment are currently unknown. Therefore we assessed the effect of early individualized dietary counseling (DC) on weight loss, major complications, and length of hospital stay (LOS) in patients with HNC. Ninety-five newly diagnosed HNC patients with (risk of) undernutrition receiving DC were compared to 95 matched HNC

Submitted 31 March 2015; accepted in final form 10 July 2015.
Address correspondence to Eva Leistra, Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center Amsterdam, PO Box 7057, 1007 MB Amsterdam, The Netherlands. Tel.: 0031 20 444 3410. Fax number: 0031 20 4444143. E-mail: e.leistra@hva.nl
Color versions of one or more of the figures in this article can be found online at www.tandfonline.com/hnuc

patients receiving usual nutritional care (UC). Difference in weight change over time was analyzed by generalized estimating equations (GEE). Differences in complications and LOS were studied by Pearson chi-squared and student's *t*-tests. Weight change between diagnosis and end of treatment was −6.0 ± 6.9% (DC) and −5.4 ± 5.7% (UC; GEE: −0.4kg, 95% confidence interval: −1.2 to 0.5; $P = 0.44$). Less DC patients experienced overall postoperative complications (44%/70%, $P = 0.04$). No effect on major postoperative or (chemo)radiotherapy complications or LOS was found. This study showed a lower prevalence of overall postoperative complications in HNC patients receiving DC but could not demonstrate an effect on weight loss, other complications, and LOS.

INTRODUCTION

Over the past decades, the recognition of disease-related undernutrition in hospitalized patients has improved in the Netherlands (1). Currently, nutritional screening is shifting toward the outpatient setting; earlier recognition of undernutrition creates the opportunity to improve a patient's nutritional status before the actual start of medical treatment. From previous research we know that the prevalence of undernutrition in outpatient departments is highest at the departments of oral maxillofacial surgery (17%) and oncology (16%) (2). This emphasizes that patients with head and neck cancer (HNC) are an important group to focus on.

HNC patients are at risk for undernutrition due to complaints induced by the tumor-localization, causing dysphagia, odynophagia, and/or oral pain (3–5). In addition, metabolic alterations induced by the tumor may result in changes in taste and appetite (6–9). Weight loss is one of the main symptoms of undernutrition. Because of these tumor-induced problems with oral intake, (critical) weight loss is observed in 3–52% of HNC patients before they start medical treatment (10–14). During treatment, weight often continues to decline due to treatment related side effects which hamper food intake even further, such as xerostomia, dysphagia, mucositis, and anorexia (6,8,15). Undernutrition is associated with loss of muscle function (16,17), impaired immune function (18), increased risk of postoperative complications (19–21), longer hospitalization (22), reduced quality of life (10,23–25), and increased mortality (26–28). Preventing decline in nutritional status prior to treatment could be a potential way to reduce these negative consequences.

A recent systematic review showed that individualized dietary counseling has positive effects on nutritional status and quality of life in HNC patients during radiotherapy when compared to no counseling or standard nutritional advice by a nurse (29). Yet, the effects of dietary counseling initiated at time of diagnosis are currently unknown.

Therefore, the aim of this study was to assess the effect of early individualized dietary counseling (initiated at the first outpatient visit) in patients with HNC on weight loss, major complications, and length of hospital stay.

MATERIALS AND METHODS

Study Design

This study was designed as an intervention study evaluating the effect of early individualized dietary counseling (DC) compared to usual nutritional care (UC) in patients with HNC in terms of weight loss, complications and length of hospital stay. Patients were treated with either radiotherapy (RT), chemoradiotherapy (CRT), or surgery (combined mandibular resection; COMMANDO), total laryngectomy (TLE) or transoral excision (TOE). Timing of data collection is described in Fig. 1, in which T0 describes first outpatient visit, T1 describes start of primary anti-tumor treatment, and T2 describes end of primary anti-tumor treatment (surgery: at hospital discharge; (chemo)radiotherapy ([C]RT): 12 weeks after the start of treatment).

Study Population

This study was part of a project to improve patient care at the outpatient department of Otolaryngology/Head & Neck Surgery of the VU University Medical Centre. As of July 2011, in all newly diagnosed HNC patients' height, weight, weight history, and oral symptoms were determined by outpatient nurses. All consecutive patients received early individualized DC if they met the following criteria: age 18 years or older; newly diagnosed with a malignant tumor in the head and neck area (oral cavity, pharynx, larynx, nasal cavity); treatment with curative intent; body mass index (BMI) <20 kg/m^2 (<65 yr) or <22 kg/m^2 (≥ 65 yr), and/or reported unintentional weight loss $\geq 5\%$ in the last 6 m, and/or experienced oral symptoms (dysphagia, chewing problems, or passage problems). Patients with benign tumors, undergoing palliative treatment, minor surgery during microlaryngoscopy (e.g., CO_2 laser), or patients not able to understand the dietary advice due to language barriers or cognitive impairment, were excluded. The study was approved by the ethical review board of the VU University Medical Center. As the study was part of a care improvement program, no written informed consent was obtained from patients.

A control group was drawn from a historical cohort of newly diagnosed HNC patients who visited the outpatient department of Otolaryngology/Head & Neck Surgery of the VUmc between June 2007 and June 2011. Patients were one-to-one matched for the following baseline characteristics; tumor location (oral cavity, oropharynx, nasopharynx, hypopharynx, larynx, nasal cavity), TNM tumor stage (I–IV), primary treatment (radiotherapy, chemoradiotherapy, surgery), nutritional screening outcome within 1 week after first outpatient visit [combination of Short Nutritional Assessment Questionnaire (SNAQ) and BMI] (30,31), sex, and age. Matching was performed blind for any outcome parameter.

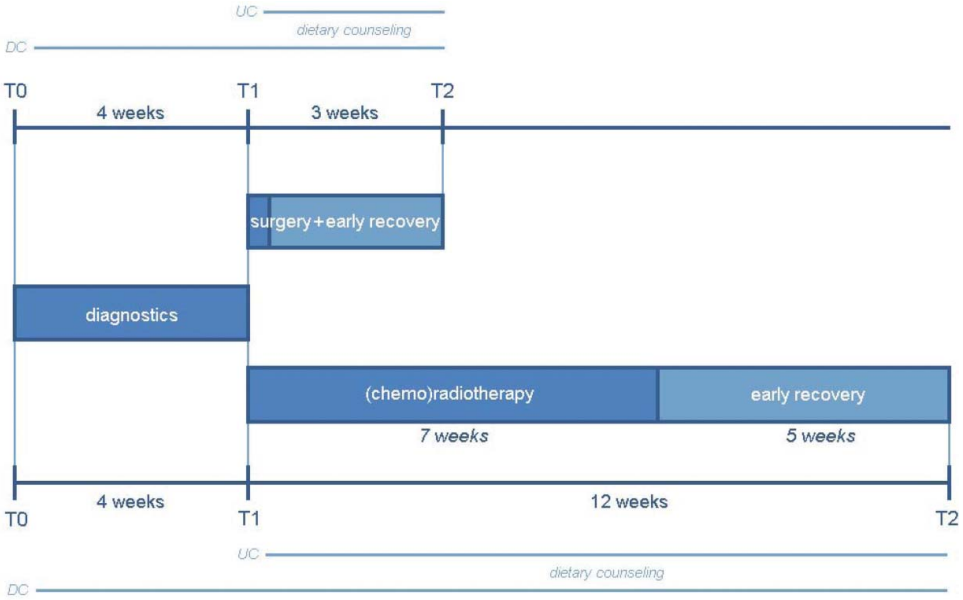

FIG. 1. Data collection on body weight for head and neck cancer patients undergoing surgery and (chemo)radiotherapy. T0 = first outpatient visit; T1 = start of primary antitumor treatment; T2 = end of primary antitumor treatment; DC = early individualized dietary counseling; UC = usual care.

Nutritional Screening

In both DC and UC patients, nutritional screening was performed by a senior nurse at T0 (during or within 1 week after first outpatient visit) using the SNAQ (30). As we recently demonstrated that SNAQ alone is an insufficient tool in detecting undernutrition in the outpatient setting, we used a combination of SNAQ screening outcome and BMI to determine nutritional status (31). Patients were classified as severely undernourished when SNAQ $\geq$ 3 and/or BMI $<$18.5 kg/m^2 ($<$65 yr) or $<$20 kg/m^2 ($\geq$65 yr); moderately undernourished when SNAQ = 2 and/or BMI ranged from 18.5 to 20 kg/m^2 ($<$65 yr) or from 20 to 22 kg/m^2 ($\geq$65 yr); and not undernourished when SNAQ $\leq$ 1 and BMI $>$20 kg/m^2 ($<$65 yr) or $>$22 kg/m^2 ($\geq$65 yr) (30–32).

Individualized DC

DC patients were consulted by a dietician within 1 wk after their first outpatient visit. Dietary counseling was provided according to the most recent Dutch guidelines (33,34) and aimed to optimize or maintain nutritional status (35).

Dietary assessment consisted of a dietary recall to determine current intake of energy, nutrients, and alcohol; an evaluation of oral symptoms affecting nutritional intake, including the shortened questionnaire on Functional Assessment of Anorexia/Cachexia Therapy (FAACT A/CS12) (36); and a complete nutritional assessment, including the measurement of weight, fat-free mass (index) measured with multi-frequency BIA, handgrip strength, and mid-upper arm (muscle) circumference. Accordingly, the dietician designed an individualized dietary advice aiming to achieve a recommended protein intake of at least 1.2–1.5 gram per kg body weight, and a recommended energy intake according to the Harris Benedict equation (37) with an individual surcharge for disease and activity (38,39).

The individualized dietary advice initially focused on improving dietary patterns with normal food intake, protein- and/or energy enrichment, modified texture in patients with dysphagia, and alleviation of oral symptoms in patients with oral pain or chewing problems. If patients did not meet their goals with normal food, oral nutritional supplements (ONS), and/or tube feeding were provided. Next to oral advice, all patients received written information, including general nutritional advice for HNC patients, advice on protein- and/or energy-enriched diet, and information on ONS or tube feeding if applicable.

In the (approximately) 4 weeks between first outpatient visit (T0) and start of antitumor treatment (T1), the dietician consulted the patients weekly by telephone or face-to-face during outpatient or diagnostic hospital visits. Consultation involved evaluation of weight, nutritional intake, and oral symptoms, and the dietician gave additional advice or adjusted the treatment strategy when necessary.

UC

The difference between DC and UC was related to timing of dietary treatment. Whereas DC patients were offered the abovementioned dietary treatment regimen in the pretreatment period, in UC patients, in general, dietary treatment was initiated at start of antitumor treatment (Fig. 1). In the UC group,

patients were prescribed ONS (standard of 4 packages a day) by the nurse in case of a SNAQ score of ≥3 or severe swallowing problems. UC patients were consulted by a dietician before start of treatment (T0–T1) only on referral by a physician.

During antitumor treatment (T1–T2), all patients (DC and UC) received protocolized dietary counseling by a dietician; weekly until discharge in patients undergoing surgery, and in Weeks 1, 3, 5, 6, 7, 9, and 12 in patients undergoing (C)RT. Frequency of dietary consultations increased when more problems occurred. Patients undergoing chemoradiotherapy underwent prophylactic percutaneous endoscopic gastrostomy placement prior to start of CRT treatment in both DC and UC groups. Tube feeding was started in case of continuing low intake.

Outcome Variables

Three outcome parameters were compared between DC and UC: weight change, major postoperative and (chemo)radiotherapy-induced complications, and length of hospital stay. Data on outcome variables were retrieved from medical records, except for body weight in the DC group.

Weight Change

Data on body weight were collected at first outpatient visit (T0), start of primary treatment (T1), and end of primary treatment (T2). In DC patients, body weight and height were measured. Height was measured to the nearest 0.5 cm using a stadiometer (Seca 222, Seca Medical Scales & Measuring Systems, Birmingham, UK) with the patients standing barefoot. In patients who were unable to stand, height was retrieved from self-reported height. Weight was measured to the nearest 0.1 kg using a calibrated electronic scale (Seca 888, Seca Medical Scales & Measuring Systems, Birmingham, UK). Patients were wearing light indoor clothes without shoes. A correction factor of −1.6 and −1.0 kg for clothes was used in men and women respectively (40). Furthermore, a correction factor of −0.4 and −0.3 kg was used in men and women respectively, when patients were unable to take off their shoes (40). In UC patients, data on height and weight were obtained from medical records and corrected for clothes and shoes when applicable.

Complications

Data on postoperative complications were systematically obtained from surgical reports, clinical patient records, and discharge letters. Patients were dichotomously classified as having a certain complication or not. Overall postoperative complications included all complications leading to a complicated postoperative course, with special regard to aspiration pneumonia, wound infections, fistulas, and major complications. Major postoperative complications were defined as malaise-related readmissions within 4 weeks after hospital discharge, reoperation due to wound healing problems or reoperation for fistula, admission to the intensive care unit (ICU), and in-hospital mortality and were all robust and well-documented in medical records. All surgical complications obtained from medical records were discussed with the head and neck surgeon (Simone E. J. Eerenstein).

Data on (C)RT complications were obtained from radiotherapy records, clinical patient records (if applicable), and discharge letters. In patients undergoing (C)RT, major complications were determined as unplanned hospital admissions during treatment, and postponement of chemotherapy. In addition, severe acute toxicity was assessed according to the Common Terminology Criteria for Adverse Events (CTCAEv3.0) as determined by the radiotherapist; mucositis ≥ Grade 3, dysphagia ≥ Grade 3 and xerostomia ≥ Grade 2 during Week 4–8 of (C)RT treatment were compared between DC and UC groups. In our center, assessment of CTCAE radiotherapy toxicity scores was introduced in 1997. For HNC patients undergoing radiotherapy, these scores are documented according to protocol; weekly during radiation for 8 weeks and at regular intervals thereafter (41).

Length of Hospital Stay

In patients undergoing surgery, length of hospital stay was recorded. Length of hospital stay is presented for the total surgical group and differentiated for type of surgery.

Statistical Analysis

Comparisons between the DC and UC group were carried out on an intention-to-treat basis, whereby DC patients were analyzed in the DC group, regardless whether they had participated in all dietary consultations.

Baseline characteristics of the DC and UC group were described using means ± SD for continuous variables, and frequencies and proportions for dichotomous and categorical variables.

Differences in body weight change over time between the DC and UC group were analyzed using generalized estimating equations with an exchangeable correlation structure, corrected for T0 weight and number of days between measurements to correct for individual variation and the differences in time span between surgery and (C)RT treatment period. Difference in weight change over time was assessed for all patients, and for subgroups based on treatment (surgery, (C)RT) and nutritional status at baseline (no undernutrition, moderate undernutrition, severe undernutrition).

Differences in complications were compared with Pearson chi-squared tests. Differences in length of hospital stay were tested with independent student's *t*-tests.

All analyses were performed using SPSS 20.0 for Windows (IBM Corp., Armonk, NY). *P* values of <0.05 were considered as statistically significant.

RESULTS

Table 1 summarizes baseline (T0) characteristics of the DC and the UC group. Groups were comparable for all baseline characteristics, except for body weight at T0. DC patients had significantly lower body weight at diagnosis compared to UC patients (67.9 ± 14.1 vs. 72.3 ± 15.9 kg; $P = 0.04$), however groups were not significantly different for BMI (23.7 ± 4.7 vs. 22.7 ± 4.4 kg/m^2; p=0.14). Twenty-one percent (DC) and 19% (UC) of patients were scheduled for radiotherapy, 43% (DC) and 45% (UC) underwent chemoradiotherapy, and 36% (both groups) underwent surgery as primary treatment.

Three DC patients never started the scheduled curative intended treatment; 2 rejected their curative intended treatment (both RT), and 1 died before start of treatment (CRT). No follow-up data are available for these patients. All UC patients started the scheduled treatment.

TABLE 1
Baseline characteristics of head and neck cancer patients receiving early individualized dietary counseling (DC) or usual care (UC)

Characteristic	DC ($n = 95$) *n*(%)	UC ($n = 95$) *n*(%)	*P* value
Sex			0.52
Male	65(68)	69(73)	
Female	30(32)	26(27)	
Age[a]	62.2 ± 10.0	60.5 ± 9.8	0.23
Weight[a]	67.9 ± 14.1	72.3 ± 15.9	0.04
Height[a]	172.8 ± 9.3	174.6 ± 8.9	0.18
BMI[a]	23.7 ± 4.7	22.7 ± 4.4	0.14
Low BMI[b]	17(18)	12(13)	0.31
Tumor location			0.99
Oral cavity	28(29)	28(29)	
Oropharynx	32(34)	32(34)	
Nasopharynx	1(1)	2(2)	
Hypopharynx	10(11)	10(11)	
Larynx	20(21)	20(21)	
Nasal cavity	4(4)	3(3)	
TNM stage			0.78
Stage I	7(7)	5(5)	
Stage II	9(10)	13(14)	
Stage III	21(22)	21(22)	
Stage IV	58(61)	56(59)	
Nutritional status			0.71
No undernutrition	40(42)	45(47)	
Moderate undernutrition	15(16)	12(13)	
Severe undernutrition	40(42)	38(40)	
Primary antitumor treatment			0.93
Radiotherapy	20(21)	18(19)	
Chemoradiotherapy	41(43)	43(45)	
Surgery	34(36)	34(36)	
COMMANDO	10(11)	10(11)	
TLE	11(12)	11(12)	
TOE	13(14)	13(14)	

BMI = body mass index; COMMANDO = combined mandibular resection; TLE = total laryngectomy; TOE = transoral excision.
[a]Mean ± SD.
[b]Low BMI: <18.5 kg/m^2 (<65 years) or <20 kg/m^2 (≥65 years)

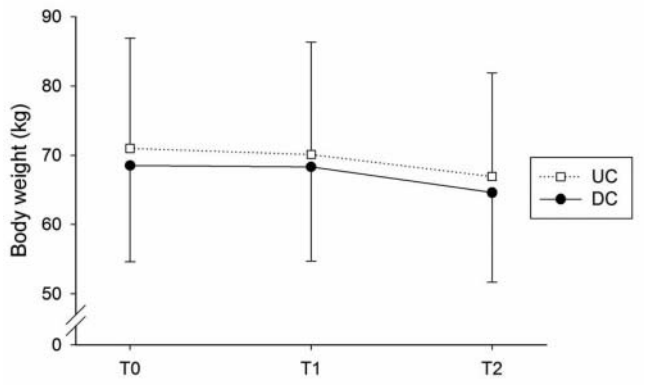

FIG. 2. Changes in body weight over time in head and neck cancer patients receiving early individualized dietary counseling (DC) or usual care (UC). T0 = first outpatient visit; T1 = start of primary antitumor treatment; T2 = end of primary antitumor treatment.

The mean period between diagnosis and start of primary antitumor treatment was on average 29 ± 9 days in the DC group and 33 ± 11 days in the UC group ($P < 0.01$). Out of the 95 DC patients, 79 were consulted by a dietician at their first visit to the outpatient department of Otolaryngology/Head & Neck Surgery, and 16 were first consulted within 1 week after this outpatient visit. One patient (RT) refused any dietary counseling after the first consultation, all other DC patients were consulted more than once between diagnosis and start of treatment. Between T0 and T1, 32 patients were prescribed ONS, and 1 patient was prescribed tube feeding.

Out of the 95 UC patients, 72 were screened for undernutrition at diagnosis, and 23 were screened within 1 week after diagnosis. In the UC group, 26 patients (27%) were referred to a dietician for at least 1 consultation between T0 and T1.

Prior to (C)RT treatment, prophylactic percutaneous endoscopic gastrostomy placement was performed in 39 DC and 36 UC patients.

Weight Change

In both groups, body weight declined during the course of treatment (Fig. 2). On average, DC patients experienced −0.7% (±5.5%) weight loss and UC patients experienced −0.2% (±3.5%) weight loss between T0 and T1 ($P = 0.53$). Only patients with moderate undernutrition at baseline gained weight between T0–T1 in both groups (2.4% ± 5.5% vs. 0.5 ± 1.8; $P = 0.25$). Between T0 and T2, DC patients experienced −6.0% (±6.9%) weight loss and UC patients experienced −5.4% (±5.7%) weight loss ($P = 0.83$). When corrected for baseline weight and number of days between measurements, no significant treatment effect for weight change was observed between DC and UC patients; the estimated difference in weight change between the groups on average over time was 0.4 lower for DC compared to UC (95% CI: −1.2–0.5; $P = 0.44$). Also for the subgroup analyses for treatment or nutritional status at baseline no significant differences were found (Table 2).

Complications

The prevalence of overall postoperative complications was significantly lower in DC patients compared to UC patients (respectively, 44% and 70%, $P = 0.04$). No significant differences were found regarding the prevalence of pneumonia, oral infections, or fistula. The prevalence of major postoperative complications was relatively low (12% vs. 18%) with no statistically significant difference between the groups (Table 3).

During (C)RT, between T1 and T2, 56% of DC and 54% of UC patients were admitted during treatment due to intake failure, malaise, impaired renal function, or dyspnea. In 28% of DC and 19% of UC patients, chemotherapy was postponed or cancelled (NS; Table 4).

The majority of patients undergoing (C)RT developed severe acute toxicity in Week 4–8 of radiotherapy. Severity

TABLE 2
Overall treatment effect of early individualized dietary counseling (DC) or usual care (UC) on changes in body weight over time for all patients and subgroups based on primary treatment and nutritional status at first outpatient visit (T0)

	β	95% CI	P value
All patients ($n = 95$)	−0.4	−1.2 to 0.5	0.44
According to primary treatment			
Surgery ($n = 34$)	0.5	−0.8 to 1.9	0.43
(C)RT ($n = 61$)	−0.9	−2.0 to 0.3	0.13
According to baseline nutritional status			
No undernutrition ($n = 40$ vs. $n = 45$)	−0.5	−1.9 to 0.9	0.48
Moderate undernutrition ($n = 15$ vs. $n = 12$)	−1.0	−2.9 to 1.0	0.32
Severe undernutrition ($n = 40$ vs. $n = 38$)	0.2	−1.1 to 1.5	0.81

β (and p value) represents the overall treatment effect on body weight over time, derived from generalized estimating equation (GEE) with an exchangeable correlation structure, adjusted for T0 weight and number of days until measurement. (C)RT = (chemo)radiotherapy.

TABLE 3
Postoperative complications and length of stay (days) in head and neck cancer patients with surgery receiving early individualized dietary counseling (DC) or usual care (UC)

	DC ($n = 34$)	UC ($n = 34$)	
	n(%)	n(%)	P value
Overall complications[a]	15(44)	21(70)	0.04
Pneumonia	1(3)	3(10)	0.24
Oral infection	2(6)	2(7)	0.90
Fistula	1(3)	2(7)	0.48
Other[b]	12(35)	15(50)	0.24
Major complications	4(12)	6(18)	0.49
Reoperation	2(6)	5(15)	0.23
Readmission <4 wk	1(3)	0(0)	0.31
ICU admission	1(3)	2(6)	0.56
In hospital mortality	0(0)	0(0)	—
LOS (days) all patients[c]	18.5 ± 11.2	19.3 ± 11.2	0.79
COMMANDO	22.9 ± 6.6	23.8 ± 9.7	0.81
TLE	26.0 ± 12.7	26.8 ± 9.4	0.87
TOE	8.9 ± 2.5	9.4 ± 5.2	0.74

LOS = length of hospital stay; COMMANDO = combined mandibular resection; TLE = total laryngectomy; TOE = transoral excision.
[a]UC: n=4 missing data on overall postoperative complications
[b]Other postoperative complications: bleeding, wound dehiscence, anastomotic leakage, intraoral necrosis, skin necrosis, decubitus (neck), refeeding syndrome, edema tongue, lung embolism, dyspnea, cardiac insufficiency, atrial fibrillation, hypertension, hypotension, wound infection donor-site free flap, free flap complication
[c]LOS in mean ± SD

of mucositis, xerostomia, and dysphagia was not significantly different between groups regarding ≥ Grade 3 mucositis, ≥ Grade 2 xerostomia and ≥ Grade 3 dysphagia (Table 4).

LOS

In both groups, 34 patients underwent surgery ($n = 10$ COMMANDO, $n = 11$ TLE, $n = 13$ TOE). No significant differences were observed between DC and UC patients regarding mean length of hospital stay for the total group (18.5 ± 11.2 compared to 19.3 ± 11.2 days ($P = 0.79$), nor when differentiated for type of surgery (Table 3).

DISCUSSION

This study aimed to determine the effect of early individualized dietary counseling in HNC patients on weight loss, major postoperative and (chemo)radiotherapy complications, and length of hospital stay. No effects on any of these primary

TABLE 4
(Chemo)radiotherapy complications in head and neck cancer patients receiving early individualized dietary counseling (DC) or usual care (UC)

	DC (n = 57)[a]		UC (n = 61)		
	n/n[b]	(%)	n/n[b]	(%)	P value
Unplanned admission	32/57	(56)	33/61	(54)	0.82
Postponement of chemotherapy	11/39	(28)	8/43	(19)	0.30
Acute toxicity[c]					
Mucositis ≥ 3	30/48	(63)	33/58	(57)	0.56
Xerostomia ≥ 2	36/47	(77)	42/59	(73)	0.53
Dysphagia ≥ 3	25/47	(53)	37/59	(63)	0.32

[a]DC = $n = 1$ died before start of treatment (CRT), $n = 1$ died in first week of treatment (CRT); $n = 2$ were allocated to RT but never started treatment.
[b]n/n = number of cases/number of patients with data on complication.
[c]Acute toxicity according to the Common Terminology Criteria for Adverse Events (CTCAEv3.0).

outcomes could be demonstrated. However, we found a significantly lower rate of overall postoperative complications in patients receiving DC.

To our knowledge, no other studies have been performed on the effectiveness of individualized dietary counseling offered in such an early stage of diagnosis. As described earlier, studies have been limited to effects of dietary counseling on nutritional status of HNC patients undergoing (C)RT during antitumor treatment (29). Three studies in patients undergoing radiotherapy showed a beneficial effect of individualized dietary counseling during treatment on weight change during treatment (42), or 12 (43), and 16 (44) weeks after commencing radiotherapy. In HNC patients undergoing surgery, studies have been performed on the effect of pretreatment nutritional support on nutritional status, complications, length of hospitalization and survival (45–50). However, these RCTs were mostly limited to a pretreatment time period less than 11 days, and most studies investigated the effect of immunonutrition only (45,46,49,50).

Apart from a significant difference in overall postoperative complications, no effects on primary outcomes could be demonstrated. The mechanism is unclear as other outcomes were not improved. The occurrence of postoperative complications could be influenced by a worsened nutritional status in terms of low protein and energy intake, but may also be dependent on other factors, such as factors related to the surgical procedure. Moreover, complications may be related to a deprived immune status caused by insufficient intake of vitamins and trace elements, frequently observed in this patient group with a high prevalence of smoking and drinking habits (51). We speculate that the quality of nutrition with regard to vitamins and trace elements was better in DC patients due to the dietetic involvement, conceivably leading to a lower risk of infections (52), but we have no data to support this hypothesis. Identifying these factors associated with clinical outcomes would provide more insight in the risk of developing weight loss or complications and the role of nutritional status and early dietary intervention in this course.

There are several possible explanations for not finding a treatment effect on the main outcomes. The additional value of dietary counseling was mainly expected to commence in the weeks between diagnosis and start of treatment, as this was the period in which DC patients were systematically consulted by a dietician according to the new treatment protocol. During antitumor treatment, all patients, both DC and UC, received the same protocoled nutritional treatment. The time of 4 weeks prior to treatment may have been too limited to improve the patients' nutritional status. In comparison, a study of van den Berg et al, comparing the effect of individualized dietary counseling and standard care between diagnosis and rehabilitation, could only demonstrate a significant difference in weight loss at 2 months after treatment (44).

Another factor explaining no treatment effect, is the fact that patients in the UC group could have had dietary counseling and/or ONS between T0 and T1 as well, making both interventions less distinguishable. In the UC group, 26 out of 95 patients had been consulted by a dietician between diagnosis and start of treatment, although their dietary counseling was not as intensive as in the DC group. Moreover, for UC patients with a SNAQ score ≥ 3 or extensive swallowing problems, ONS were prescribed by the senior nurse who had performed the screening. Thirty UC patients had a SNAQ score ≥ 3, and subsequently should have been prescribed ONS, but this number could have been higher. In the DC group, comparable numbers were found; 32 patients were prescribed ONS and one patient was prescribed tube feeding initiated by the dietician at first outpatient visit.

Ravasco et al. (53) showed that during RT treatment in HNC patients, providing individualized dietary counseling is more effective than adding ONS to the regular diet on nutritional intake, nutritional status, oral symptoms and quality of life in medium term (3 months after end of RT). However, a statistically significant increase in both energy (>300 kcal/day) and protein (>35 g/day) intake was observed in short term (between start and end of RT) in the ONS group (53). Prescribing ONS to our UC population may have increased the nutritional intake, and therefore reduced the contrast in dietary intervention between the two groups and could explain the fact that no differences were found on main outcomes.

A major strength of this study is the thorough matching procedure based on 6 different criteria and blinded for any outcome parameter. By matching intervention patients to patients treated for the same health problems in the past, we created two comparable groups at baseline, with regard to gender, age, BMI, tumor location, TNM stage, nutritional status, and primary treatment.

There are also several limitations of the study design that need to be discussed. First, as this study was started as a project to improve patient care, we compared our prospectively included DC cohort to a historical cohort of carefully matched patients receiving usual care. Patients in the DC group were included in the study when they had a low BMI, weight loss, or if they were at risk of undernutrition due to oral symptoms (dysphagia, chewing problems, or passage problems). Accordingly, all 40 DC patients who were not undernourished according to the classification of SNAQ + BMI, did experience any of these oral symptoms. For patients in the UC group, information on oral symptoms could not structurally be obtained from medical records, so we did not use this as a matching criterion. As patients were matched for the same tumor types and stages, a comparable distribution of oral symptoms was expected. However, as this could not be confirmed by data, UC patients with no undernutrition according to SNAQ + BMI at baseline may have been in a better nutritional condition than those in the DC group.

Secondly, we were partly dependent on data reported in medical records (radiotherapy records, surgical reports and discharge letters). The absence of a treatment effect on weight change may also be related to the method of data collection. Whereas in DC patients weight was measured at all moments, in UC patients, weight could have been measured or recalled. At T0, weight was measured in 31% of UC patients, although this was 74% at T1. From literature it is known that overweight persons tend to underestimate their weight, whereas underweight persons tend to overestimate their weight (54,55). Consequently, relative weight change in UC patients may be biased, but we cannot state toward what direction.

Thirdly, because of the retrospective design, we were unable to compare data regarding changes in muscle mass and muscle strength between groups, as these measurements were not routinely carried out in the historical cohort. Weight loss reflects both loss of fat mass and loss of fat free mass. Finding no significant differences in weight loss does not imply that muscle mass did not change significantly (50,56). Distinguishing between these components gives more insight in a patient's nutritional and physical condition. A better condition (e.g., better lean mass) could be associated with less complications, less tiredness of energy, but also a better quality of life or better survival (57).

Therefore, in future research, a prospective design is recommended to assess changes in body weight, muscle mass, and muscle strength. It would also be worthwhile to study the effects on quality of life.

There is a growing body of evidence that dietary treatment during antitumor treatment has beneficial effects on nutritional status and quality of life (29,58). We therefore expect that dietary treatment initiated at diagnosis would be beneficial as well, but this has not been studied sufficiently. Moreover, there is still no international consensus on the optimal form and timing of nutritional support in this patient group (59,60).

As dietary counseling during treatment is standard care in the Netherlands and several other countries (58,60), and in most centers dietary counseling in the pretreatment period becomes standard care as well, it could be discussed whether performing a RCT to assess the effectiveness of dietary treatment will be ethical. We therefore advise to focus on identifying risk profiles (which patients do benefit most from the provided intervention?) to establish and evaluate an individualized approach.

In conclusion, this study could not demonstrate an effect of early individualized dietary counseling compared to usual care in patients with HNC on weight loss, major surgical, and (C)RT complications and length of hospital stay, but showed a lower prevalence of overall postoperative complications. A plausible explanation for this limited effect is the minimal contrast between DC and UC. This study is the first to assess the effect of early dietary intervention in HNC patients, and provides a basis for further research.

ACKNOWLEDGMENTS

The authors thank Paula Weppner, Anouk Lenzen, and Jacqueline Pos for their cooperation in data collection, and all nurses from the outpatient department of Otolaryngology/ Head & Neck Surgery, with special regard to Machteld van Driel, for performing the nutritional screening.

FUNDING

This study was funded by institutional funds.

REFERENCES

1. Leistra E, van Bokhorst-de van der Schueren MA, Visser M, van der Hout A, Langius JA, et al.: Systematic screening for undernutrition in hospitals: predictive factors for success. *Clin Nutr* **33**, 495–501, 2013.
2. Leistra E, Neelemaat F, Evers AM, van Zandvoort MHWM, Weijs PJM, et al.: Prevalence of undernutrition in Dutch hospital outpatients. *Eur J Intern Med* **20**, 509–513, 2009.
3. Jager-Wittenaar H, Dijkstra PU, Vissink A, van der Laan BF, van Oort RP, et al.: Critical weight loss in head and neck cancer-prevalence and risk factors at diagnosis: an explorative study. *Support Care Cancer* **15**, 1045–1050, 2007.
4. Larsson M, Hedelin B, Johansson I, and Athlin E: Eating problems and weight loss for patients with head and neck cancer: a chart review from diagnosis until one year after treatment. *Cancer Nurs* **28**, 425–435, 2005.
5. Colangelo LA, Logemann JA, and Rademaker AW: Tumor size and pretreatment speech and swallowing in patients with resectable tumors. *Otolaryngol Head Neck Surg* **122**, 653–661, 2000.
6. Baracos VE: Cancer-associated cachexia and underlying biological mechanisms. *Annu Rev Nutr* **26**, 435–461, 2006.
7. Richey LM, George JR, Couch ME, Kanapkey BK, Yin X, et al.: Defining cancer cachexia in head and neck squamous cell carcinoma. *Clin Cancer Res* **13**, 6561–6567, 2007.
8. Silver HJ, Dietrich MS, and 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* **29**, 893–900, 2007.
9. Van Cutsem E and Arends J: The causes and consequences of cancer-associated malnutrition. *Eur J Oncol Nurs* **9**(Suppl 2), S51–S63, 2005.
10. Capuano G, Gentile PC, Bianciardi F, Tosti M, Palladino A, et al.: Prevalence and influence of malnutrition on quality of life and performance status in patients with locally advanced head and neck cancer before treatment. *Support Care Cancer* **18**, 433–437, 2010.
11. Isenring E, Bauer J, and Capra S: The scored Patient-Generated Subjective Global Assessment (PG-SGA) and its association with quality of life in ambulatory patients receiving radiotherapy. *Eur J Clin Nutr* **57**, 305–309, 2003.
12. Langius JA, Doornaert P, Spreeuwenberg MD, Langendijk JA, Leemans CR, et al.: Radiotherapy on the neck nodes predicts severe weight loss in patients with early stage laryngeal cancer. *Radiother Oncol* **97**, 80–85, 2010.
13. Matthews TW, Lampe HB, and Dragosz K: Nutritional status in head and neck cancer patients. *J Otolaryngol* **24**, 87–91, 1995.
14. van den Berg MG, Rasmussen-Conrad EL, Gwasara GM, Krabbe PF, Naber AH, et al.: A prospective study on weight loss and energy intake in patients with head and neck cancer, during diagnosis, treatment and revalidation. *Clin Nutr* **25**, 765–772, 2006.
15. Chencharick JD and Mossman KL: Nutritional consequences of the radiotherapy of head and neck cancer. *Nat Rev Cancer* **51**, 811–815, 1983.

16. Argiles JM: Cancer-associated malnutrition. *Eur J Oncol Nurs* **9**(Suppl 2), S39–S50, 2005.
17. Norman K, Stobaus N, Zocher D, et al.: Cutoff percentiles of bioelectrical phase angle predict functionality, quality of life, and mortality in patients with cancer. *Am J Clin Nutr* **92**, 612–619, 2010.
18. van Bokhorst-de van der Schueren MAE, Von Blomberg-van der Flier BME, Riezebos RK, Scholten PET, Quak JJ, et al. Differences in immune status between well-nourished and malnourished head and neck cancer patients. *Clin Nutr* **17**, 107–111, 1998.
19. Guo CB, Zhang W, Ma DQ, Zhang KH, and Huang JQ: Hand grip strength: an indicator of nutritional state and the mix of postoperative complications in patients with oral and maxillofacial cancers. *Br J Oral Maxillofac Surg* **34**, 325–327, 1996.
20. Salas S, Deville JL, Giorgi R, Pígnon T, Bagarry D, et al.: Nutritional factors as predictors of response to radio-chemotherapy and survival in unresectable squamous head and neck carcinoma. *Radiother Oncol* **87**, 195–200, 2008.
21. van Bokhorst-de van der Schueren MAE, van Leeuwen PA, Sauerwein HP, Kuik DJ, Snow GB, et al.: Assessment of malnutrition parameters in head and neck cancer and their relation to postoperative complications. *Head Neck* **19**, 419–425, 1997.
22. Pressoir M, Desné S, Berchery D, Rossignol G, Poiree B, et al.: Prevalence, risk factors and clinical implications of malnutrition in French Comprehensive Cancer Centres. *Br J Cancer* **102**, 966–971, 2010.
23. Langius JA, van Dijk AM, Doornaert P, Kruizenga HM, Langendijk JA, et al.: More than 10% weight loss in head and neck cancer patients during radiotherapy is independently associated with deterioration in quality of life. *Nutr Cancer* **65**, 76–83, 2013.
24. Ravasco P, Monteiro-Grillo I, Vidal PM, and Camilo ME: Cancer: disease and nutrition are key determinants of patients' quality of life. *Support Care Cancer* **12**, 246–252, 2004.
25. van den Berg MG, Rasmussen-Conrad EL, van Nispen L, van Binsbergen JJ, and Merkx MA: A prospective study on malnutrition and quality of life in patients with head and neck cancer. *Oral Oncol* **44**, 830–837, 2008.
26. Datema FR, Ferrier MB, and Baatenburg de Jong RJ: Impact of severe malnutrition on short-term mortality and overall survival in head and neck cancer. *Oral Oncol* **47**, 910–914, 2011.
27. Van Bokhorst-de van der Schueren MAE, Van Leeuwen PAM, Kuik DJ, Klop WM, Sauerwein HP, et al. The impact of nutritional status on the prognoses of patients with advanced head and neck cancer. *Nat Rev Cancer* **86**, 519–527, 1999.
28. Nguyen TV and Yueh B: Weight loss predicts mortality after recurrent oral cavity and oropharyngeal carcinomas. *Nat Rev Cancer* **95**, 553–562, 2002.
29. Langius JAE, Zandbergen MC, Eerenstein SEJ, van Tulder MW, Leemans CR, et al.: Effect of nutritional interventions on nutritional status, quality of life and mortality in patients with head and neck cancer receiving (chemo)radiotherapy: a systematic review. *Clin Nutr* **32**, 671–678, 2013.
30. Kruizenga HM, Seidell JC, de Vet HC, Wierdsma NJ, and van Bokhorst-de van der Schueren MA: Development and validation of a hospital screening tool for malnutrition: the Short Nutritional Assessment Questionnaire (SNAQ). *Clin Nutr* **24**, 75–82, 2005.
31. Leistra E, Langius JA, Evers AM, van Bokhorst-de van der Schueren MAE, Visser M, et al.: Validity of nutritional screening with MUST and SNAQ in hospital outpatients. *Eur J Clin Nutr* **67**, 738–742, 2013.
32. Sergi G, Perissinotto E, Pisent C, Buja A, Maggi S, et al.: An adequate threshold for body mass index to detect underweight condition in elderly persons: the Italian Longitudinal Study on Aging (ILSA). *J Gerontol A Biol Sci Med Sci* **60**, 866–871, 2005.
33. Vogel J, Beijer S, Doornink N, and Wipkink A: *Handboek voeding bij kanker* (*Handbook Nutrition and Cancer*). Utrecht, The Netherlands: De Tijdstroom; 2012.
34. Comprehensive Cancer Centers (IKNL): *General Nutrition and Dietary Treatment* (2.0). 2012. http://www.oncoline.nl/general-nutrition-and-dietary-treatment
35. Arends J, Bodoky G, Bozzetti F, Fearon K, Muscaritoli M, et al.: ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology. *Clin Nutr* **25**, 245–259, 2006.
36. Ribaudo JM, Cella D, Hahn EA, et al.: Re-validation and shortening of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire. *Qual Life Res* **9**, 1137–1146, 2001.
37. Roza AM and Shizgal HM: The Harris Benedict equation reevaluated: resting energy requirements and the body cell mass. *Am J Clin Nutr* **40**, 168–182, 1984.
38. Dutch Institute for Healthcare Improvement CBO: *Guideline Perioperative Nutrition*. Utrecht, The Netherlands: Dutch Institute for Healthcare Improvement CBO, 2007.
39. Sauerwein HP and Strack van Schijndel RJ: Perspective: How to evaluate studies on peri-operative nutrition? Considerations about the definition of optimal nutrition for patients and its key role in the comparison of the results of studies on nutritional intervention. *Clin Nutr* **26**, 154–158, 2007.
40. Frank E and Dunlop AL: What does a patient's outfit weigh? *Fam Med* **32**, 595–596, 2000.
41. Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, Leemans CR, Aaronson NK, et al.: Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. *J Clin Oncol* **26**, 3770–3776, 2008.
42. Macia E, Moran J, Santos J, Blanco M, Mahedero G, et al.: Nutritional evaluation and dietetic care in cancer patients treated with radiotherapy: prospective study. *Nutrition* **7**, 205–209, 1991.
43. Isenring EA, Capra S, and Bauer JD: Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. *Br J Cancer* **91**, 447–452, 2004.
44. van den Berg MG, Rasmussen-Conrad EL, Wei KH, Lintz-Luidens H, Kaanders JH, et al.: Comparison of the effect of individual dietary counselling and of standard nutritional care on weight loss in patients with head and neck cancer undergoing radiotherapy. *Br J Nutr* **104**, 872–877, 2010.
45. Buijs N, van Bokhorst-de van derSchueren MA, Langius JAE, Leemans CR, Kuik DJ, et al.: Perioperative arginine-supplemented nutrition in malnourished patients with head and neck cancer improves long-term survival. *Am J Clin Nutr* **92**, 1151–1156, 2010.
46. Felekis D, Eleftheriadou A, Papadakos G, Bosinakou I, Ferekidou E, et al.: Effect of perioperative immuno-enhanced enteral nutrition on inflammatory response, nutritional status, and outcomes in head and neck cancer patients undergoing major surgery. *Nutr Cancer* **62**, 1105–1112, 2010.
47. Paccagnella A, Morello M, Da Mosto MC, Baruffi C, Marcon ML, et al.: Early nutritional intervention improves treatment tolerance and outcomes in head and neck cancer patients undergoing concurrent chemoradiotherapy. *Support Care Cancer* **18**, 837–845, 2010.
48. Rabinovitch R, Grant B, Berkey BA, Raben D, Ang KK, et al.: Impact of nutrition support on treatment outcome in patients with locally advanced head and neck squamous cell cancer treated with definitive radiotherapy: a secondary analysis of RTOG trial 90-03. *Head Neck* **28**, 287–296, 2006.
49. Snyderman CH, Kachman K, Molseed L, Wagner R, D'Amico F, et al.: Reduced postoperative infections with an immune-enhancing nutritional supplement. *Laryngoscope* **109**, 915–921, 1999.
50. van Bokhorst-de van der Schueren MA, Quak JJ, von Blomberg-van der Flier BM, Kuik DJ, Langendoen SI, et al.: Effect of perioperative nutrition, with and without arginine supplementation, on nutritional status, immune function, postoperative morbidity, and survival in severely malnourished head and neck cancer patients. *Am J Clin Nutr* **73**, 323–332, 2001.
51. Maggini S, Wintergerst ES, Beveridge S, and Hornig DH: Selected vitamins and trace elements support immune function by strengthening

epithelial barriers and cellular and humoral immune responses. *Br J Nutr* **98**(Suppl 1), S29–S35, 2007.

52. Wintergerst ES, Maggini S, and Hornig DH: Contribution of selected vitamins and trace elements to immune function. *Ann Nutr Metab* **51**, 301–323, 2007.
53. Ravasco P, Monteiro-Grillo I, Marques VP, and Camilo ME: Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. *Head Neck* **27**, 659–668, 2005.
54. Connor Gorber S, Tremblay M, Moher D, and Gorber B: A comparison of direct vs. self-report measures for assessing height, weight and body mass index: a systematic review. *Obes Rev* **8**, 307–326, 2007.
55. Haverkort EB, de Haan RJ, Binnekade JM, and van Bokhorst-de van der Schueren MA: Self-reporting of height and weight: valid and reliable identification of malnutrition in preoperative patients. *Am J Surg* **203**, 700–707, 2012.
56. Weed HG, Ferguson ML, Gaff RL, Hustead DS, Nelson JL, et al.: Lean body mass gain in patients with head and neck squamous cell cancer treated perioperatively with a protein- and energy-dense nutritional supplement containing eicosapentaenoic acid. *Head Neck* **33**, 1027–1033, 2011.
57. Baracos V and Kazemi-Bajestani SM: Clinical outcomes related to muscle mass in humans with cancer and catabolic illnesses. *Int J Biochem Cell Biol* **45**, 2302–2308, 2013.
58. Clinical Oncological Society of Australia: *Evidence Based Guidelines for the Nutritional Management of Adult Patients with Head and Neck Cancer*. Accessed on http://wiki.cancer.org.au/australia/COSA:Head_and_neck_nutrition_guidelines/
59. Brown T, Banks M, Hughes B, Kenny L, Lin C, et al.: Protocol for a randomized controlled trial of early prophylactic feeding via gastrostomy versus standard care in high risk patients with head and neck cancer. *BMC Nurs* **13**, 17, 2014.
60. Brown T, Findlay M, von Dincklage J, Davidson W, Hill J, et al.: Using a wiki platform to promote guidelines internationally and maintain their currency: evidence-based guidelines for the nutritional management of adult patients with head and neck cancer. *J Hum Nutr Diet* **26**, 182–190, 2013.