Support Care Cancer (2010) 18:433–437
DOI 10.1007/s00520-009-0681-8

ORIGINAL ARTICLE

Prevalence and influence of malnutrition on quality of life and performance status in patients with locally advanced head and neck cancer before treatment

Giorgio Capuano · Pier Carlo Gentile · Federico Bianciardi · Michela Tosti · Anna Palladino · Mario Di Palma

Received: 19 January 2009 / Accepted: 10 June 2009 / Published online: 29 June 2009

Abstract
Goals of work The aim of this study was to evaluate the prevalence and influence of malnutrition (unintentional weight loss ≥5% in the last 3 months) on quality of life (QoL) and performance status (PS) in head and neck cancer patients (HNC) before treatment.
Patients and methods Sixty-one consecutive outpatients affected by locally advanced HNC (III–IVA stage) were enrolled. In all patients, nutritional intake (by diet history), nutritional status (Patient Generated Subjective Global Assessment), unintentional weight loss (UWL), serum prealbumin, hemoglobin level (Hb), C-reactive protein, QoL (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C-30 v. 3.0), and PS (Eastern Cooperative Oncology Group (ECOG) PS) were assessed before radio or concomitant chemoradiotherapy.
Main results Thirty-six percent of HNC were malnourished before treatment. The median ECOG PS in malnourished patients was 1 (0–2), whereas in nonmalnourished was 0 (0–2; $p=0.018$). Physical ($p=0.043$), role ($p=0.047$), and social functions ($p=0.024$) scores were significantly worse in malnourished than in nonmalnourished HNC. Fatigue ($p<0.001$), appetite loss ($p<0.001$), and nausea and vomiting ($p=0.002$) scores were worse in malnourished patients than in nonmalnourished. In the multivariate analysis, UWL and Hb level independently influenced physical ($p=0.002$; $p=0.005$), role ($p=0.004$; $p=0.001$), and social functions ($p=0.024$; $p=0.009$).
Conclusion Our data suggest that an early and intensive nutritional support might reduce weight loss before, during, and after treatment completion, improving outcome, QoL, and PS.

Keywords Head and neck cancer · Weight loss · Malnutrition · Quality of life · Performance status · Nutritional support

Introduction

Malnutrition influences quality of life (QoL) and performance status (PS) in cancer patients [1, 2]. Although nutritional deterioration is common in head and neck cancer (HNC), its earliest indicator, represented by involuntary loss of body weight (UWL), is frequently underestimated or completely ignored before treatment [3, 4]. The aim of this study was to evaluate the prevalence of malnutrition in HNC and the possible influence of nutritional status on QoL and PS before radio or concomitant chemoradiotherapy.

Materials and methods

Sixty-one consecutive outpatients (69% males, 31% females), median age 50 (range 18–70) with locally advanced HNC (stage III and IVA disease), treated at Roma Saint Peter Hospital Oncology Department, were enrolled. Criteria for eligibility included absence of diabetes, hepatic or renal

G. Capuano (✉)
Clinical Nutrition Unit, Ospedale San Pietro—Fatebenefratelli,
Via Cassia,
600-00189 Rome, Italy
e-mail: giorgio.capuano@fastwebnet.it

P. C. Gentile · F. Bianciardi · M. Tosti · A. Palladino · M. Di Palma
Oncology Department, Ospedale San Pietro—Fatebenefratelli,
Rome, Italy

failure, alcohol dependence, and not previous surgical or oncological treatment. Characteristics of patients are described in Table 1 and cancer location and stage of disease in Table 2. All patients were evaluated for malnutrition (UWL), nutritional intake (by diet history), nutritional status (Patient Generated Subjective Global Assessment (PG-SGA) score), serum prealbumin (PREA; n.v. 20–40 mg/dL), hemoglobin level (Hb; n.v. 12.0–15.0 g/dL), C-reactive protein (CRP; n.v. 0.01–5.0 mg/dL), QoL (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C-30 v. 3.0), and Eastern Cooperative Oncology Group performance status scale (ECOG PS) before treatment.

Statistical analysis

For statistical analysis, we used SPSS for Window, release 13.0. The end point was to investigate the prevalence of malnutrition and the possible influence of nutritional status on QoL and PS before treatment. UWL, PG-SGA, CRP, PREA, Hb, QoL, and PS in not malnourished and malnourished patients were compared with chi-square, Fisher or T-Student tests, as appropriate. All the possible correlations were analyzed with nonparametric Spearman test. Possible influence of malnutrition on QoL and PS was tested with multivariate analysis. Significance was reported at the conventional $p<0.05$ level.

Results

Baseline differences in not malnourished and malnourished patients are described in Table 3.

Table 1 Characteristics of patients

Male, no. (%)	42 (69)
Female, no. (%)	19 (31)
Median age (range), years	50 (18–70)
Median BMI (range), kg/m^2	24.4 (16.5–32.7)
Malnourished patients[a], %	36
Mean weight loss ± SD, %	10±5
Median PG-SGA score (range)	3 (1–16)
Mean hemoglobin level ± SD (mg/dL)	13.4±1.2
Mean CRP level ± SD (mg/dL)	9.1±14.6
Mean serum prealbumin ± SD (mg/dL)	26±5
Median ECOG PS score (range)	0 (0–2)
Alcoholism	0

BMI body mass index, *PG-SGA* Patient Generated Subjective Global Assessment, *CRP* C-reactive protein, *ECOG PS* Eastern Cooperative Oncology Group performance status scale

[a] Weight loss ≥5% in the last 3 months

Table 2 Cancer location

Oropharynx	21
Oral cavity	19
Nasopharynx	13
Larynx	5
Maxillary sinus	2
Submandibular gland	1
Tumor stage	
III (%)	28
IVa (%)	72

Malnutrition

The European Society for Clinical Nutrition and Metabolism considered malnourished a patient who involuntary lost a 5% or greater of body weight in the last 3 months [5]. Thirty-six percent of patients were malnourished before treatment. Mean value ± standard deviation (SD) of UWL was 10±5 kg. Weight loss was CRP-related ($p=0.001$).

Nutritional intake

Nutritional intake was derived from a diet history. Both energy and protein intakes were analyzed at enrolment. At baseline, 10% of nonmalnourished HNC referred a reduction of usual food intake vs 67% of malnourished. Only two patients reduce food intake because of odynophagia.

Nutritional status

Nutritional status was assessed with Ottery's PG-SGA. A score of 0–1 does not require an intervention, but a reassessment on routine and regular basis during treatment. A score of 2–3 requires a patient and family education by dietician, nurse, or other clinician. A score of 4–8 requires the intervention by dietician and a score ≥9 indicates a critical need for improved symptom management and/or nutrient intervention options. In nonmalnourished HNC mean ± SD PG-SGA score was 3±2 and in malnourished 9±5 ($p=0.001$). PG-SGA score was UWL ($p<0.001$) and CRP-related ($p<0.001$).

Inflammatory status

We considered significant a CRP level ≥10 mg/dL (n.v. 0.01–5.0 mg/dL). At enrolment, in 27% of HNC, CRP level was ≥10 mg/dL. In nonmalnourished patients, mean ± SD CRP level was 4.3±5.0 mg/dL, whereas in malnourished was 20.3±22.5 mg/dL ($p=0.004$). Seventy-one percent of HNC with CRP level ≥10 mg/dL were malnourished vs 13% with CRP level <10 mg/dL.

Table 3 Baseline differences in nonmalnourished and malnourished patients

Variable	Nonmalnourished (n=36)	Malnourished (n=25)	p value*
Sex, no. of patients			–
Males	26	16	
Females	10	9	
Median age (range), years	49 (18–69)	61 (45–70)	–
Mean BMI ± SD, kg/m^2	26.1±4.7	21.1±2.7	0.006
Mean weight loss ± SD, %	1±1	11±6	<0.001
Mean PG-SGA ± SD score (range)	3±2	9±5	<0.001
Mean serum prealbumin ± SD (20–40 mg/dL)	28±5	22±3	<0.001
Mean CRP ± SD (0.1–5.0 mg/dL)	4.3±5.0	20.3±22.5	0.004
Mean hemoglobin level ± SD (mg/dL)	13.7±0.9	12.4±1.2	<0.001
Median ECOG PS (range)	0 (0–2)	1 (0–2)	0.018

BMI body mass index, *CRP* C-reactive protein, *PG-SGA* Patients Generated Subjective Global Assessment, *ECOG PS* Eastern Cooperative Oncology Group performance status scale

*p<0.050 are given only when they were significant

Serum prealbumin

At baseline in all HNC, the mean value ± SD of PREA (n.v. 20–40 mg/dL) was 26±5 mg/dL. In nonmalnourished patients, mean value ± SD was 28±5 mg/dL, whereas in malnourished was 22±3 mg/dL (p<0.001). PREA was weight loss- (p=0.001), CRP- (p=0.021), and PG-SGA-related (p=0.006).

Hemoglobin

Mean ± SD hemoglobin level in nonmalnourished was 13.7± 0.9 mg/dL and in malnourished 12.4±1.2 mg/dL (p<0.001). Hemoglobin level was weight loss- (p<0.001), CRP- (p= 0.019), and PG-SGA-related (p=0.002). In Table 4, we reported the mean concentrations of hemoglobin as measured in the subgroups of patients.

Performance status

At enrolment, the median score of ECOG PS in non-malnourished HNC was 0 (0–2), whereas in malnourished was 1 (0–2; p=0.018). PS was weight loss- (p=0.002), Hb- (p=0.042), PREA- (p=0.040), CRP- (p=0.033), and PG-SGA-related (p=0.007).

Quality of life

The mean ± SD of EORTC QLQ-C30 scores for nonmalnourished and malnourished patients are listed on Table 5. About function scales, physical (p=0.043), role (p=0.047), and social functions (p=0.024) scores were significantly better in nonmalnourished than in malnourished HNC. About symptom scales and symptoms single items, fatigue (p<0.001), appetite loss (p<0.001), and nausea and vomiting (p=0.002) scores were worse in malnourished than in nonmalnourished HNC. In the multivariate analysis, malnutrition (UWL) and Hb level independently influenced physical (p=0.002; p=0.005), role (p=0.004; p=0.001), and social functions (p=0.024; p=0.009).

Discussion

The importance of malnutrition as comorbid condition in HNC undergoing radiotherapy or concomitant chemoradiotherapy has long been recognized. Although a nutritional deterioration is reported to affect 25–50% of HNC before any therapy [6], few studies evaluated the possible prevalence and impact of malnutrition on performance and quality of life in these cancer patients before treatment. In

Table 4 Concentration of hemoglobin in the subgroups of patients

Subgroup	Hemoglobin level (g/dL)	p value*
Stable body weight + normal CRP level	13.4±0.9 (11.7–15.7)	
Stable body weight + CRP level ≥10 mg/dL	13.8±1.0 (12.2–15.5)	–
Weight loss + CRP level <10 mg/dL	12.9±0.8 (12.0–14.3)	–
Weight loss + CRP level ≥10 mg/dL	11.7±1.1 (10.6–14.1)	<0.001

Data are given as mean ± SD and range

CRP C-reactive protein

*p≤0.050 are given only when they were significant

Table 5 Mean ± SD QLQ-C30 scores in nonmalnourished and malnourished patients

Items	Nonmalnourished	Malnourished	*p* value*
Function scale			
Physical function	92±8	85±8	0.043
Role function	86±16	72±19	0.047
Emotional function	75±23	66±25	–
Social function	86±20	67±20	0.024
Cognitive function	89±17	91±17	–
Symptoms scales			
Fatigue	5±7	20±12	<0.001
Pain	7±9	13±14	–
Nausea and vomiting	3±11	21±18	0.002
Symptoms single items			
Dyspnea	3±10	13±20	–
Insomnia	17±23	30±26	–
Appetite loss	11±22	48±24	<0.001
Constipation	3±10	0±0	–
Diarrhea	3±10	13±20	–
Financial difficulties	9±19	4±11	–
Global health status	69±20	58±17	–

*$p<0.050$ are given only when they were significant

our study, we excluded HNC affected by alcoholism, 7% of HNC in our casuistry, because a heavy alcohol intake may influence independently the nutritional status; it has been estimated that the impact of malnutrition is 70% in alcoholic patients vs 30% in nonalcoholic [7]. Our data confirm that malnutrition is common also in nonalcoholic HNC not only during but also before treatment. In our experience, 36% of patients were already malnourished at enrolment; 13% of HNC with a CRP level <10 mg/dL were malnourished because of a food intake reduction due to psychological problem or, in two patients, to odynophagia, and 71% of patients with a CRP level ≥10 mg/dL were malnourished because food intake reduction was due to early satiety and severe anorexia. In this second group of patients, the presence of unintentional weight loss, anorexia, early satiety, fatigue, and inflammatory status demonstrated that about 30% of HNC might be already affected by cancer cachexia before treatment [8]. In cachectic HNC, we also founded a significant correlation between weight loss, systemic inflammation, and hemoglobin level. The possible mechanism involved in this relationship could be that both weight loss and low hemoglobin level might be considered a cytokine-mediated disorder, resulting from complex interactions between tumor cells and host [9]. Overexpression of proinflammatory cytokines (interleukin (IL)-6, IL-1β, tumor necrosis factor-α) and CRP, due to IL-6 increase, results in shortened survival of red blood cells, suppression of erythroid progenitor cells, impaired iron utilization, and inadequate erythropoietin production [10]. However, even if systemic inflammation is considered the major cause of cancer-related anemia before chemo- and radiotherapy, in our experience, statistical analysis showed that in the subgroup of patients, the hemoglobin significantly reduced only when inflammatory status was associated with weight loss [11]. Weight loss, anemia, and inflammatory status already may compromise functional ability of HNC before the treatment-induced toxicity. In addition to weight loss prior to the diagnosis, the patient may lose an additional 10% of pretherapy body weight during treatment. A total weight loss reduction ≥20% significantly correlates with treatment interruption, infections, early mortality, hospital readmission rate after treatment completion, and survival [12–18]. Since the optimal therapy for cancer-related malnutrition is curing the underlying cancer [19], our experience suggests that an early and concomitant nutritional support may stop or counteract further weight loss and improve outcome in HNC [20]

Acknowledgments We are grateful to the oncologists and nursing of the Oncological Department of San Peter Hospital in Rome. There were no grants or funding for this work. There was no conflict of interest.

References

1. Ravasco P, Monteiro Grillo I, Marques Vidal P, Camilo ME (2003) Nutritional deterioration in cancer: the role of disease and diet. Clin Oncol 15:443–450
2. Ravasco P, Monteiro Grillo I, Marques Vidal P, Camilo ME (2004) Cancer disease and nutrition are keys determinants of patients' quality of life. Support Care Cancer 12:246–252

3. Dewys WD, Begg C, Lavin PT et al (1980) Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. Am J Med 69(4):491–497
4. Laviano A, Meguid MM (1996) Nutritional issues in cancer management. Nutrition 12:358–371
5. ESPEN (2004) Basic in clinical nutrition, 3rd edn. House Galén, Prague
6. Mekhail TM, Adelstein D, Rybicki LA et al (2001) Enteral nutrition during the treatment of head and neck carcinoma. Cancer 91(9):1785–1790
7. Martin Villares C, Dominguez Calvo J, San Roman Carbajo J et al (2004) Heavy alcohol intake, malnutrition and head and neck cancer patients. Nutr Hosp 19(6):348–352
8. Skipworth RJE, Stewart GD, Dejoing CHC, Preston T, Fearon KCH (2007) Pathophysiology of cancer cachexia: much more than host–tumour interaction? Clinical Nutrition 26:667–676
9. Dicato M (2003) Anemia in cancer. Oncologist 8:19–21
10. Birgegard G, Aapro MS, Bokemeyer C et al (2005) Cancer-related anemia: pathogenesis, prevalence and treatment. Oncology 68 (1):3–11
11. Capuano G, Pavese I, Satta F et al (2008) Correlation between anemia, unintentional weight loss and inflammatory status on cancer-related fatigue and quality of life before chemo and radiotherapy. E-SPEN Eur e-J Clin Nutr Metab 3:e147–e151
12. Martin Villares C, San Roman Carbajo J, Fernandez Pello ME et al (2003) Nutritional status in head and neck cancer patients: the impact on the prognoses. Nutr Hosp 18(2):91–94
13. Beaver ME, Matheny KE, Roberts DB, Myers JN (2001) Predictors of weight loss during radiation therapy. Otolaryngol Head Neck Surg 125(6):645–648
14. Ravasco P, Monteiro Grillo I, Camilo ME (2003) Does nutrition influence quality of life in cancer patients undergoing radiotherapy? Radiotherapy Oncol 67:213–220
15. van den Berg MG, Rasmussen-Conrad EL, van Nispen L et al (2008) A prospective study on malnutrition and quality of life in patients with head and neck cancer. Oral Oncol 44(9):830–837
16. Akst LM, Chan J, Elson P, Saxton J, Strome M, Adelstein D (2004) Functional outcomes following chemo radiotherapy for head and neck cancer. Otolaryngol Head Neck Surg 131 (6):950–957
17. Colasanto JM, Prasad P, Nash MA, Decker RH, Wilson LD (2005) Nutritional support of patients undergoing radiation therapy for head and neck cancer. Oncology 19(3):371–379
18. Capuano G, Grosso A, Gentile PC et al (2008) Influence of weight loss on outcomes in patients with head and neck cancer undergoing concomitant chemo and radiotherapy. Head Neck 30:503–508
19. Laviano A, Meguid MM, Inui A et al (2005) Therapy insight: cancer anorexia–cachexia syndrome. When all you can eat is yourself. Nat Clin Pract Oncol 2(3):158–165
20. Ravasco P, Moteiro Grillo I, Marques Vidal P, Camilo ME (2005) Impact of nutrition on outcome: a prospective randomised controlled trial in patients with head and neck cancer undergoing radiotherapy. Head Neck 27:659–668