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Detailed Dietary Assessment in Patients with Inoperable Tumors: Potential Deficits for Nutrition Care Plans

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ABSTRACT

Advanced cancer often results in reduced dietary intake; however, data on actual intake at the time of diagnosis are limited. In the present study, a detailed dietary intake assessment was performed in patients with metastatic lung and upper gastrointestinal cancer, before initiation of systemic therapy. Basic demographics and performance status (PS) were recorded. Nutritional status was evaluated through anthropometry, Mini Nutritional Assessment (MNA), and 3 nonconsecutive 24-hour dietary recalls. Of the 84 patients enrolled, 61.4% were protein, energy, or protein–energy undernourished, regardless of body mass index (BMI) or MNA category. No differences in energy, macronutrients, and micronutrients intakes across BMI categories were recorded. Very low consumption of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), irrespective of energy intake, tumor site, BMI category, or PS was found. Suboptimal micronutrients intakes were recorded even in well-nourished and overweight/obese patients. Patients with adequate PS and better MNA score reported significantly higher intake of certain macro- and micronutrients (all $P < 0.05$). Most patients exhibited reduced dietary intake in terms of energy, macronutrient, and micronutrient. Very low EPA and DHA intake was recorded for the whole sample, whereas micronutrient suboptimal intakes were also prevalent in well-nourished or overweight patients. All the above should be taken into account during patients' nutritional care.

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Introduction

Malnutrition is clinically defined as a condition of imbalance of energy and nutrient intake, which leads to alterations of tissue/body composition and function, and is associated with adverse clinical outcomes (Elia M, 2003). The incidence of cancer-related malnutrition, in particular, ranges between 40 and 80% (Isenring et al., 2003; Tong et al., 2009) depending on the tumor's type and stage (Muscaritoli et al., 2006).

Cancer patients, especially those with advanced disease, do not usually consume an adequate diet as a consequence of a variety of medical, somatic, psychological, and social factors (Strasser, 2003). In their case, malnutrition could be developed either in the context of cancer cachexia, a syndrome characterized by progressive loss of muscle mass (with or without loss of fat mass) (Fearon et al., 2011) and/or it could be caused by secondary contributive factors like treatment-related toxicity (Erkurt et al., 2000), obstruction of the alimentary tract (Fearon et al., 2013), or the development of uncontrolled symptoms (i.e., depression, fatigue, and pain) (Bye et al., 2013). Evidently, primary cancers of the lung and the upper gastrointestinal (GI) track are at particular nutritional risk (Muscaritoli et al., 2006). Evidence suggests that disease-related malnutrition is a major cause of morbidity and mortality (Van Cutsem and Arends, 2005) and, when cancer is considered, it is additionally associated with poor response to treatment and quality of life (Gupta et al., 2006; Paccagnella et al., 2011).

In many countries, some form of nutritional screening/assessment is recommended for all newly diagnosed cancer patients, in the context of a multidisciplinary approach. However, patients are usually referred to dietitians when malnutrition is clinically apparent or by the time they enter a palliative care setting; hence, this condition is often underestimated, especially in overweight/obese patients (Gioulbasanis et al., 2015). Furthermore, as there are no standard established criteria to define malnutrition, various indexes are proposed to identify nutritional risk such as weight loss history, body mass index (BMI), ideal body weight percentage, or their combinations (Martin et al., 2015). Alternatively, nutritional

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screening tools, like Patient-Generated Subjective Global Assessment (PG-SGA) and MNA that provide a more detailed evaluation, are also used to classify patients into risk groups (Blum and Strasser, 2011).

Ideally, those patients deemed to be at risk or malnourished should be further referred for detailed nutritional assessment, including thorough assessment of dietary intake, followed by nutritional intervention/support (nutrition care plan) (Huhmann and Cunningham, 2005). Up to now, practice and research have primarily focused on the evaluation of energy–protein intake and supplementation (Baldwin et al., 2011, Menon et al., 2014), as well as administration of particular dietary components, like eicosapentaenoic acid (EPA), and certain micronutrients either separately or within hypercaloric formulas (Gullett et al., 2011; Uster et al., 2013).

Available data regarding the dietary consumption of the aforementioned nutrients of cancer patients are relatively limited. Most studies focused on the assessment of macronutrient dietary intake in various primaries at any time during the cancer trajectory (Hutton et al., 2006; Pistoia et al., 2012), while there are very few studies evaluating the micronutrient intake (Gomez Valiente da Silva et al., 2014; Menon et al., 2014), especially at the time of diagnosis (Menon et al., 2014). To the best of our knowledge, no studies so far assessed the dietary intake of long-chain omega-3 fatty acids, namely EPA and DHA. The aim of this study was to comprehensively evaluate detailed dietary intake in patients with inoperable primaries of the lung and the upper GI tract, at baseline, and to compare them with the recommended dietary reference intakes (Institute of Medicine, 2011). The associations between macro- and micronutrients intake and BMI classification, performance status (PS), and MNA were additionally evaluated.

Methods

Eligibility

Patients with inoperable primaries of the lung and the upper GI tract, referred for initiation of systemic antineoplastic therapy to the Department of Medical Oncology of the University Hospital of Larissa, from April 2012 to February 2013, were eligible. Patients were older than 18 years and had histologically and/or cytologically proven tumors.

Patients with a history of a second primary tumor (except nonmelanoma skin tumor)—those underwent a major surgical operation within the past 3 months, those with symptoms severely interfering with the process of food intake and those not able to collaborate for the collection of information relevant to nutritional assessment and/or those planned to receive radiotherapy only as first-line antineoplastic therapy—were excluded.

The study was approved by the Ethics and Scientific Committee of the Institution and was carried out in accordance with the Declaration of Helsinki (World Medical Association, 1997). All subjects were informed about the aims and procedures of the study and gave their written consent.

Baseline demographics and clinical characteristics

Basic demographics (date of assessment, gender, age, and smoking status) and detailed medical history, concomitant medication, the presence of active infection and disease-related characteristics (primary site, tumor stage, and the presence of visceral and/or central nervous system metastasis) were recorded at baseline. PS was assessed according to the Eastern Cooperative Oncology Group (ECOG) (Oken et al., 1982). In addition, the presence of symptoms that could potentially affect food intake (before the onset of the systemic therapy) (i.e., xerostomia, smell and/or taste alterations, dysphagia, early satiety, nausea/vomiting, abdominal pain, and other) were recorded. The patients were further grouped (based on these symptoms) into 2 categories: none or oligo-symptomatic, i.e., having none to 2 symptoms and those who reported $\geq$ 2 symptoms.

Nutritional assessment

Anthropometry

Body weight (BW) was measured with a digital scale ($\pm$0.1 kg), in light clothing, without shoes after assessing for the presence of edema or ascites. Standing height was measured without shoes with a stadiometer ($\pm$0. cm) with the shoulders in relaxed position, arms hanging freely, and head oriented in the horizontal plane (Frankfort horizontal plane). BMI was then calculated as weight (kg)/height (m^2) and patients were classified based on their BMI as underweight (BMI $<$ 18.5 kg/m^2), normal weight (18.5 $\leq$BMI $<$ 25 kg/m^2), overweight (25 $\leq$BMI $<$ 30 kg/m^2), and obese (BMI $\geq$ 30 kg/m^2) according to the World Health Organization (WHO) criteria (WHO, 1998). For the purpose of statistical analysis patients were also grouped into 2 BMI categories, namely underweight and normal weight versus overweight and obese. Self-declared BW changes in the preceding 3 months were recorded and the % BW change was calculated.

Nutritional screening

Nutritional screening was based on the MNA. Briefly, MNA is an 18-item questionnaire validated originally for use in elderly patients with nonmalignant diseases

(Guigoz et al., 1996) and later adapted as an integral part of Comprehensive Geriatric Assessment of oncologic patients (Extermann and Hurria, 2007). We have previously reported that MNA has better predictive value than weight loss history in patients with metastatic primaries of the lung and that it could also discriminate nutritional risk in overweight/obese cancer patients with metastatic primaries of the lung and the upper GI, irrespective of age (Gioulbasanis et al., 2011; Gioulbasanis et al., 2015). Questions are divided into two main groups: those of screening and of assessment (Huhmann and Cunningham, 2005). Screening consists of questions related to changes in oral intake, weight loss, mobility, stress, and BMI. A score of <11 out of 14 suggests risk of malnutrition or already malnourished malnutrition and is the cut point for the full assessment, which additionally includes medical history, specific questions on eating habits, and measurements of arm and calf circumferences. A total score is then calculated (maximum 30 points); a score of >23.5 points denotes adequate nutritional status, a score of 17.0–23.5 indicates risk of malnutrition, and a score of <17 indicates malnutrition (Guigoz et al., 1996). All patients underwent full assessment.

Dietary assessment

Three nonconsecutive 24-hour (24-h) dietary recalls were recorded before the first treatment cycle by a trained dietitian through telephone interviews with either the patient or a caregiver. Patients were informed that in the following days a dietitian would call them 3 times to record the previous day's dietary intake. Subjects did not know the exact day the researcher would call, for eliminating intentional changes in the diet. During the 24-h dietary recall, each subject recalled and described in detail all types and amounts of foods and beverages consumed in the previous 24 hours on three separate occasions: two weekdays and one weekend day. Data from the three 24-h recalls were analyzed for their energy, and macro- and micronutrient contents, by Nutritionist Pro version 2.2 software (Axxya Systems-Nutritionist Pro®), and their mean was calculated. The Nutritionist Pro® food database was expanded by adding analyses of traditional Greek foods and recipes (Trichopoulou and Georga, 2004) and nutrient information of oral nutritional supplements as provided by manufacturers.

Energy (kcal) and protein (gr) intake were converted to kcal/kg and g/kg BW, actual or adjusted depending on patient's BMI. Specifically, for patients with a BMI <20 kg/m^2 an adjusted BW which corresponds to a BMI = 20 was used, whereas for patients with 20 ≥ BMI ≤ 25 their actual weight was used. For patients with a BMI > 25 we used the adjusted BW as calculated from the following equation: ideal body weight (IBW) + [(actual weight–IBW) × 25%], whereas IBW was considered the weight that corresponded to a BMI of 25 kg/m^2 (Dietitian/Nutritionists from the Nutrition Education Materials Online, "NEMO", team, 2012; Wright and Jones, 2010). For the evaluation of the energy intake, the recommendation of 30 kcal/kg BW was used as a cut-off (Arends et al., 2006) of the minimum requirement for ambulant patients. Patients with an energy intake <30 kcal/kg BW were classified as having inadequate intake (undernourished) and those with an intake of ≥30 kcal/kg were classified as well-nourished. The reference value of 1 g/kg for protein intake (Arends et al., 2006) was considered as the minimum requirement for adult patients. Patients with an intake of <1 g/kg were classified as having inadequate intake (undernourished) and those with an intake of ≥ 1g/kg were classified as well-nourished. Four groups were subsequently created: 1) Energy undernutrition: inadequate energy and adequate protein intake; 2) Protein undernutrition: inadequate protein and adequate energy intake; 3) Energy–protein undernutrition: inadequate protein and energy intake; and 4) Well-nourished: adequate protein and energy intake.

In order to evaluate patient's micronutrient intake, the estimated average requirement (EAR) and the Dietary Reference Intake Values [Recommended daily allowance (RDA) or Adequate Intake (AI)] by age and sex were used (Institute of Medicine, 2011). An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97–98 percent) healthy individuals in a group, while an EAR is the average daily nutrient intake level estimated to meet the requirements of half of the healthy individuals in a group (Institute of Medicine, 2011). Although these EARs and RDAs are primarily defined for healthy populations, they have also been used in cancer patients (Arends et al., 2006), in the lack of other evidence-based recommendations tailored to cancer patient needs.

Statistical analysis

Statistical analysis was performed using SPSS (SPSS for Windows, version 21.0, SPSS, Chicago, IL). Normality of the distribution of the variables investigated was assessed using normality probability plots. Continuous variables (normal distributed) are presented as means ± standard deviation (SD), continuous variables (not normally distributed) as medians (25th, 75th percentiles) and categorical variables as absolute frequencies. The $\chi 2$ test evaluated the associations between categorical variables. Differences in median values between groups were analyzed with the Mann–Whitney U test for comparison of

2 groups and the Kruskal–Wallis test for comparison of 4 groups.

Results

In total, 92 consecutive patients were evaluated and 84 (91.3%) of them agreed to be enrolled in the study. Patients' characteristics at baseline are presented in Table 1. Median age for the population was 67.1 years and the majority (72.6%) had lung cancer primaries. Sixty (72.3%) patients experienced weight loss during the past 3 months; among them, 43 (74.1%) reported weight loss of <10% and 15 (25.9%) reported weight loss of ≥10%. Six patients (7.2%) had a stable weight and 17 patients (20.5%) gained weight, during this preceding period. Even before the onset of chemotherapy, 75 (89.3%) patients already experienced nutrition impact symptoms that could potentially interfere with food intake. Specifically, 42.9% of patients reported anorexia, 20.2% smell alterations, 31% taste alterations, 22.6% dysphagia, 34.5% early satiety, 26.2% pain, 35.7% constipation, 12.3.% diarrhea, and 45.2% xerostomia. Forty-two (50%) patients were non- or oligo-symptomatic, while the other half were considered as having a heavy burden of symptoms.

Regarding BMI, only 3.6% of patients were classified as underweight, whereas half of the study sample was classified as overweight/obese. According to the MNA, 33 (41.8%) patients had adequate nutritional status, 38 (48.1%) were at risk of malnutrition, and 8 (10.1%) were malnourished. Due to low number of malnourished patients in our sample, we further classified patients into 2 groups: those with an adequate nutritional status (no risk) (33, 41.8%) and those at risk or already malnourished grouped together (at risk/malnutrition) (46, 58.2%) for statistical comparisons. The prevalence of at risk/presence of malnutrition differed significantly between the two primary cancer site groups ($P = 0.046$) with 52% of lung cancer patients versus 78.3% of gastric cancer patients being at risk or already malnourished.

For the total sample, the median (25th and 75th percentile) for energy and protein intake was 1857 (1391, 2278) kcal/day and 84 (59, 103) g/day, respectively. When energy and protein intakes were expressed per kilograms of BW, their medians were 27 (19, 33) kcal/kg BW and 1.2 (0.8, 1.4) g/kg BW, respectively. With regard to energy–protein undernutrition, as assessed by the patients' compliance to the recommended energy and protein intake, 61.4% of patients were protein, energy, or protein–energy undernourished (i.e., 22 [26.5%] were energy-undernourished, 1 [1.2%] was protein-undernourished, and 28 [33.7%] were protein–energy undernourished). The presence of undernutrition (i.e., energy, protein, and energy–protein undernutrition) did not differ between BMI groups or between the 2 groups of primary cancer site (i.e., lung vs. upper GI), but tended to differ between the 2 MNA groups, with those at risk/malnourished having higher % of undernutrition ($P = 0.08$) as well.

Table 2 depicts energy and macronutrient intake in the whole sample and between the two primary cancer site groups. In general, patients consumed high-fat diets, with monounsaturated fats being the main source of fat, whereas long-chain n-3 fatty acids intakes, namely EPA and DHA, were extremely low and dietary fiber intake was nearly 50% of that recommended in the healthy population (Institute of Medicine, 2011). Compared to lung cancer patients, those with upper GI primaries had a lower daily energy intake ($P = 0.03$), mainly due to lower fat intake ($P = 0.01$).

In Table 3, micronutrient intake in the whole sample through food consumption, as well as the corresponding EARs and RDAs and the percentage of patients with intakes lower than the recommended, is presented. For those micronutrients with different EARs and RDAs per sex, the intakes for males and females are presented separately in Table 3. The prevalence of micronutrients suboptimal intakes was high for the majority of the vitamins and minerals assessed. The micronutrients intake was further explored according to the primary cancer site

Table 1. Demographic, medical, and anthropometric parameters of the participants.

Variable	Values
Study sample (N)	84
Sex	
Males	70 (83.3%)
Age (yrs)	67.1 ± 8.2
Primary site	
Lung	61 (72.6%)
Gastric	23 (27.4%)
Stage	
3	13 (15.5%)
4	71 (84.5%)
Performance status	
0–1	58 (71.6%)
≥2	23 (28.4%)
BMI (kg/m^2)	25.2 ± 13.9
BMI categories	
Underweight	3 (3.6%)
Normal weight	38(45.2%)
Overweight	30 (35.7%)
Obese	13 (15.5%)
MNA groups	
Adequate nutritional status	33(39.3%)
Risk of malnutrition	38(45.2%)
Malnutrition	8(9.5%)
Presence of any symptom(s) related with food intake	
Non-/oligo-symptomatic (0–2 symptoms)	42 (50%)
Heavy symptom burden (>2)	42 (50%)

Values are presented as n (%), mean ± SD
BMI: Body mass index, MNA: Mini Nutritional Assessment

Table 2. Energy and macronutrient intake in the whole sample and according to primary cancer site groups.

	Total sample	Lung cancer	Gastric cancer	*P* value
Energy (kcal/d)	1857(1391,2277)	1941 (1453, 2444)	1665 (1211, 1994)	0.034
Proteins (g/d)	84 (60, 103)	86 (61, 106)	72 (53, 95)	0.072
Proteins (% of daily energy)	17 (15, 20)	17 (15, 20)	18 (15, 20)	0.393
Carbohydrates g/day	186 (150, 240)	203 (153, 254)	169 (122, 229)	0.101
Carbohydrates (% of daily energy)	42 (36, 48)	42 (36, 48)	43 (37, 49)	0.633
Dietary fibers g/day	15 (9, 20)	16 (9, 24)	13 (9, 17)	0.132
Fats g/day	84 (59, 105)	88 (68, 109)	67 (47, 94)	0.012
Fat (% of daily energy)	41 (36, 44)	42 (37, 45)	39 (34, 44)	0.196
SFA (% of daily energy)	13 (10, 15)	12(10, 15)	13(11, 14)	0.707
MUFA (% of daily energy)	19 (16, 23)	19 (16, 23)	17 (16, 22)	0.130
PUFA (% of daily energy)	5(4, 6)	5 (4, 6)	4 (3, 5)	0.093
EPA mg/d	5 (2, 83)	7 (2, 85)	3 (1, 14)	0.301
DHA mg/d	29 (1, 222)	31 (1, 231)	11 (0, 154)	0.370

SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

(lung vs. upper GI). Compared to GI patients, lung cancer patients had higher vitamin B1 [1.9 (1.4, 2.7) vs. 1.4 (1.3, 1.8), $P = 0.03$] and folate intake [567 (415,759) vs. 346 (283,454), $P = 0.02$].

When dietary intake analysis for EPA, DHA, and micronutrients was limited to those who were well-nourished, based on their compliance with energy and protein recommendations, intakes lower than the EAR of calcium (25%), folate (5.6%), vitamins C (28.1%) and B6 (18.8%), and zinc (18.8%) were recorded. EPA and DHA (mg/d) medians, 25th and 75th percentiles, were 13 (2–128) and 64 (9–357), respectively. We also aimed to explore micronutrient deficiencies and EPA and DHA intake, restricting the analysis to the group of overweight/obese patients. Specifically, a lower intake than the EAR was reported for vitamins B12 (9.5%), B1 (19%), B6 (42.9%) and A (19%), calcium (50%), folate (38.1%), and zinc (42.9%). EPA and DHA (mg/d) medians, 25th and 75th percentiles, were 5 (1–80) and 27 (0–207), respectively.

When differences in the dietary intakes of energy, macronutrients, and micronutrients were explored according to the MNA categories (no risk vs. at risk/malnutrition), patients with no risk compared to those at risk/malnourished had a significant higher intake of energy (Kcal/d) (1941 vs. 1665, $P = 0.04$), fat (g/d) (93 vs. 77, $P = 0.03$), dietary fibers (g/d) (15.6 vs. 13.1, $P = 0.04$), vitamins B1 (mg/d) (1.6 vs. 1.2, $P = 0.02$) and B6 (mg/d) (1.7 vs. 1.4, $P = 0.02$), folate (μcg/d) (418 vs. 304, $P = 0.01$), and zinc (mg/d) (10.7 vs. 8.4, $P = 0.02$). In addition, patients with ECOG PS of $\leq$1 had a significant higher intake of protein (g/d) [87 (63–105) vs. 69(40–89), $P = 0.03$], dietary fibers (g/d) [16 (10–21) vs. 10 (5–16), $P = 0.01$], polyunsaturated fatty acid (PUFA) (% of daily energy) [5 (4–6) vs. 4 (3–5), $P = 0.02$], vitamin C (mg/d) [118 (67–162) vs. 47 (18–97), $P = 0.03$], vitamin B1 (mg/d) [1.4 (1.0–1.9) vs. 1.1 (0.7–1.6), $P = 0.03$], vitamin B12 (mcg/d) [4.1 (2.7–6.8) vs. 3.5 (1.7–4.5), $P = 0.04$], and selenium (mcg/d) [105 (74–130) vs. 82 (56–113), $P = 0.03$], respectively.

Finally, across the 2 categories of patients who were none-/oligo-symptomatic and with heavy symptom burden at baseline, a statistically significant different intake was found only for particular micronutrients intake,

Table 3. Micronutrient intake and comparison to estimated average requirements (EARs) and recommended dietary allowances (RDAs) in the whole sample.

	EAR (males/females)	RDA (males/females)	Intake median (25th, 75th percentile)	Intake< EAR (%) (males/females)	Intake< RDA (%) (males/females)
Fat-soluble vitamins					
Vitamin A (μcg/d), (males/females)	625/500	900/700	1597 (560, 2943)/2041 (396, 2438)	25.7/30.8	40.8/30.8
β-carotene (μcg/d)	—	—	1778 (489, 3880)	—	—
Water-soluble vitamins					
Vitamin C (mg/d), (males/females)	75/60	90/75	96 (49, 156)/61 (27, 130)	35.7/46.2	43.7/53.8
Vitamin B1 (mg/d), (males/females)	1/0.9	1.2/1.1	1.4 (1.0, 1.8)/0.8 (0.7, 1.2)	21.4/53.8	26.8/66.7
Vitamin B6 (mg/d), (males/females)	1.4/1.3	1.7/1.5	1.6 (1.1, 2.2)/1.1 (0.8, 1.4)	37.1/76.9	55.7/83.3
Vitamin B12 (mcg/d)	2	2.4	3.8 (2.6, 6.1)	15.7	98.8
Minerals					
Calcium (mg/d)	1000	1200	953 (591, 1280)	51.8	70.2
Folate (μcg/d)	320	400	326 (199, 472)	47.0	64.3
Zinc (mg/d), (males/females)	9.4/6.8	11/8	9 (7,14)/8 (6,9)	48.6/38.5	100/53.8
Selenium (μcg/d)	45	55	95 (69, 123)	8.4	14.3

namely in vitamins C (mg/d) [125(68–181) vs. 74 (28–125), $P = 0.004$], B6 (mg/d) [1.8 (1.3–2.4 vs. 1.3(0.8–1.8), $P = 0.003$], and B12 (mcg/d) [5.2 (3.0–7.8) vs. 3.5 (2–4.9), $P = 0.01$] as well as zinc (mg/d) [10.7(8–14.8) vs. 8.3(5–12), $P = 0.02$] and selenium (mcg/d) [105 (81–138) vs. 84 (59–115), $P = 0.02$]. No differences in dietary intake were found between BMI categories.

Discussion

In this study, baseline macro- and micronutrient dietary intakes were comprehensively evaluated in a mixture of inoperable cancer patients being at increased risk for malnutrition. Indeed, more than 70% of patients reported unintentional weight loss in the preceding 3 months and almost 90% experienced at least one symptom that could potentially interfere with the process of food intake. Consequently, a high prevalence of undernutrition was found, with more than 60% of patients being protein, energy, or protein–energy undernourished, evaluated by the compliance to energy and protein recommendations, regardless of BMI or MNA category. With regard to micronutrients dietary intake, the prevalence of suboptimal intake was high for the majority of the vitamins and minerals assessed, even when dietary intake analysis was limited to well-nourished patients, i.e., those consuming adequate amount of energy and proteins and/or those who are overweight or obese.

The importance of energy and protein intake is well established (Cawood et al., 2012) and maintaining an adequate intake is instrumental in helping prevent a further deterioration in nutritional status. Previous studies have assessed the dietary intake of oncological patients, mainly focusing on energy and macronutrients intake. Specifically, dietary energy intakes of patients with advanced malignant disease have been previously reported (Bauer et al., 2005a; Bauer and Capra, 2005b; Bosaeus et al., 2001; DeWys et al., 1981; Fearon et al., 2003; Menon et al., 2014; Vidal-Casariego et al., 2015) with average energy intakes ranging between 22 and 24 kcal/kg/day, while higher intakes (25→35 kcal/kg BW) seem to be required for weight maintenance (Baracos, 2006). Regarding protein intakes, previous studies reported a protein intake of <1.5 g/kg/day (Hutton et al., 2006; Vidal-Casariego et al., 2015). In our study, mean energy and protein intake were estimated at 27 kcal/kg/day and 1.2 g/kg/day, respectively, and 6 out of 10 patients did not reach the goal for energy and/or protein intake, showing a compromised dietary intake even before the initiation of the systematic anticancer therapy.

In addition, a very low consumption of long-chain n-3 fatty acids, namely EPA and DHA, irrespective of energy intake, tumor site, BMI category, or PS was found, although the sample came from a Mediterranean country. At the moment, there are no recommendations for optimal intake levels of EPA and DHA in cancer patients, but studies suggest that n-3 fatty acid intake may result in specific benefits, such as anticachectic properties, improved quality of life, weight maintenance and weight gain, and perhaps enhancement of the effects of some treatments (Gogos et al., 1998; Hardman, 2004). Although these findings are not entirely consistent, and more research is needed (Maclean et al., 2005; Vaughan et al., 2013), current results indicate the need for assessment of long-chain n-3 fatty acids intake and the potential need for supplementation.

According to the present results, a substantial proportion of patients exhibited suboptimal micronutrient intakes based on the EARs for healthy individuals, even when the analysis was restricted to well-nourished and overweight/obese patients. Although there are limited studies assessing micronutrient intake in oncological patients, their findings also reveal a high prevalence of micronutrient deficiencies (Gomez Valiente da Silva et al., 2014; Menon et al., 2014). Studies comparing micronutrient status between cancer patients and healthy individuals revealed that cancer patients have lower levels of vitamins A, B, C, D, and E, as well as selenium and zinc (Strohle et al., 2010; Whiteside et al., 2004). Micronutrient deficits may in turn be associated with increased risk for complications after surgery, depression, and compromised immune competence that influence the clinical outcomes and quality of life of cancer patients (Menon, 2014). In clinical practice, given the lack of evidence-based recommendations, the proposed intakes for healthy individuals are also applied for cancer patients, although these patients might have different needs in several micronutrients and especially in those with antioxidant and anti-inflammatory properties.

Although no differences in the dietary intake were noticed across BMI categories, when patients were stratified according to MNA, significant differences in dietary intake were observed. However, in routine oncology practice, BMI is generally used and when patients are classified as overweight or obese, they tend to be considered as well-nourished and thus they do not typically receive regular nutritional assessment. As previously shown, BMI might not be an appropriate tool to guide decisions regarding nutritional support as these patients may be equally malnourished (Gioulbasanis et al., 2015) or sarcopenic (Prado et al., 2008; Tan et al., 2009). On the contrary, present findings support that classification according to MNA or PS categories may better reflect risk for undernutrition. This finding deserves further study both in patients with advanced and early stages of

the disease, because it could improve the nutritional risk assessment procedures in cancer patients. Furthermore, based on the results of the present study there is a need for early referral of patients with advanced cancer for detailed nutritional assessment and potential nutritional intervention/support (nutrition care plan), which could improve nutritional intake (Baldwin et al., 2012; Kiss et al., 2014), aspects of quality of life (Baldwin et al., 2012), as well as nutritional status (Langius et al., 2013).

Our study has strengths and limitations. One of our study's strength is that there are a very few studies exploring the dietary intake of cancer patients at the time of diagnosis, in terms of both macro- and micronutrients intake. Moreover, assessment of dietary intake was based on triplicate 24-h recalls reflecting in a quite objective way the actual intake. Nevertheless, recall bias and underreporting during the 24-h recalls cannot be ruled out. Another limitation was the lack of biomarkers (e.g., serum micronutrients concentrations) that could give a more thorough description of the subjects' nutritional status.

In conclusion, based on the present study, a high percentage of cancer patients exhibit poor nutritional intake and/or risk of or malnutrition, already at the time of diagnosis. Nutritional deficits concerned energy intake, macronutrients, as well as several minerals and vitamins, whereas those in better PS and nutritional status, based on the MNA, declared more appropriate dietary intake. Regarding the EPA and DHA, very low consumption was recorded irrespective of energy intake, tumor site, BMI category, or PS. According to these results, enrichment of the usually prescribed hypercaloric formulas with EPA and other micronutrients seems to be justifiable in order to reassure that the daily recommended intakes are met. The findings of the present study also deserve further investigation in other types and stages of cancer.

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