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Original Article

Nutrient Intake and Nutritional Status in Hungarian Gynecological Cancer Patients

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Summary. *Aims:* The incidence of malignant diseases is on the rise. Although nutrition and nutritional status do not get enough attention in the therapy of gynecological tumors, they may affect mortality and morbidity. More information on nutrient intake and nutritional status of gynecological cancer patients are needed to provide generalizable advice. The primary aim of our study was to analyze the nutrient intake, risk of malnutrition and quality of life among Hungarian gynecological cancer patients. *Methods:* We used a 3-day food record in order to assess energy and nutrient intake. The Malnutrition Universal Screening Tool was used to establish malnutrition risk, and the quality of life was evaluated using the EORTC-QLQ-C30 questionnaire. We included one hundred ninety-five gynecological oncology patients diagnosed with cervical, endometrial or ovarian cancer in our study. *Results:* Based on our results malnutrition risk affects 39% of gynecological oncology patients at the time of diagnosis, while this rate is considerably higher among patients under treatment. Furthermore, the intake of most micronutrients was less than the recommended dose, regardless of the status of the disease. Also, we found the quality of life to be strongly related to malnutrition risk. *Conclusions:* The study suggests that early detection of malnutrition risk and nutritional interventions are necessary among Hungarian gynecological cancer patients to helping improve nutrition intake, nutrition status and quality of life.

Key words: Cancer, Dietary intake, Malnutrition risk, Nutritional status

Introduction

Cervical cancer is the fourth most common cancer in women, with an estimated 528 000 new cases, and there were an estimated 266 000 deaths from cervical cancer worldwide in 2012. Endometrial cancer is the sixth most common cancer in women, with an estimated 320 000 new cases and 76 000 deaths worldwide, while ovarian cancer was the seventh most common cancer in women with 239 00 new cases and 152 000 deaths worldwide in 2012 (1). As a result of the development of nutrition science, it has increasingly become clear that health-conscious diet has an important role both in the prevention and in the treatment of cancer. Cancer treatments are continually developing. However, the frequent development of tumor or treatment-induced malnutrition and disturbed metabolism often hampers successful treatment outcomes in cancer patients (2). Nutrition and nutritional status may affect the mortality and morbidity of gynecological tumors. Therefore, more research should aim to explore this field (3). It is known that 50-80% of cancer patients are affected by malnutrition; however, it is largely dependent on the type of the tumor, the stage of the disease, and the therapeutic interventions (4). At the time of diagnosis, 20% of gynecological cancer patients are affected by malnutrition (3). Furthermore, malnutrition is responsible for at least 20% of deaths in cancer (3,4). Malnutrition or insufficient nutritional status may have detrimental consequences. It indicates a worse prognosis, reduces the chances of successful anticancer therapy, and worsen the quality of life. Many factors may directly lead to reduced food intake and thereby insufficient energy intake, such as nausea, changes in the sense of taste, while other factors may indirectly influence food intake, e.g.fatigue, and pain.

Moreover, weight loss in cancer patients can also be attributed to the side effects of anticancer treatment, including chemotherapy, radiotherapy, and surgery. Also, upregulated and activated cytokines play an essential role in metabolic and endocrine changes, and catabolic pathways are activated. Metabolic changes affect both proteins, carbohydrates and fat metabolisms (4).

There is a lack of information on the nutrient intake and nutritional status of gynecological cancer patients in Hungary. The objective of this study was to assess the nutrient intake, risk of malnutrition of patients in early (I-II) and advanced (III-IV) stage of gynecological cancer, and also, among patients before treatment, during primary treatment or treatment of cancer recurrence and examine the quality of life among Hungarian gynecological cancer patients.

Materials and Methods

The study subjects included 195 adults (≥ 18-year-old) female patients diagnosed with cervical cancer (n=65), endometrial cancer (n=40) or ovarian cancer (n=90). We grouped our patients according to the tumor stage, early (I-II), or advanced (III-IV). On the other hand, they were also categorized according to their disease status as follows: Group-1: patients at the time of the diagnosis of gynecological cancer before any therapeutic interventions; Group-2: patients during primary treatment, i.e., during adjuvant chemo/radiotherapy following surgery; Group-3: patients during the treatment of cancer recurrence. Thirty-one % of the patients were in early, and 69% of the patients were in an advanced stage of the tumor. The study intervention was performed at the time of diagnosis in 47% of cases, during primary treatment in 28% of cases, and at the time of tumor recurrence in 25% of the patients. The study was performed at the Department of Obstetrics and Gynecology, the University of Debrecen between 2016 and 2018. The study protocol was approved by the local Institutional Ethics Committee (ETT-TUKEB license: 18424-2/2016/EKU 0430/16).

A questionnaire was used to record personal data and anthropometric status. We calculated the Body Mass Index (BMI) as usual, from a weight (kg)/height $(m)^2$ ratio. We assessed the BMI by WHO classifications (5). We also considered it essential to measure waist circumference, because independent of general obesity, which generally assesses as BMI, central obesity was associated with the risk of several cancers (6). Waist circumference measurement was carried out halfway between the top of the hip blade and the lower rib edge (7). In order to assess malnutrition risk, we used a complex screening method, the' Malnutrition Universal Screening Tool' (MUST). It is a reliable and valid screening tool to establish the risk of malnutrition, considering three factors; BMI, undesirable weight loss, and the impact of the disease on appetite and food intake (8). The EORTC-QLQ-C30 general quality of life measurement questionnaire which is internationally accepted to measure the quality of life (QoL) in cancer patients. This questionnaire consists of 30 items divided into three symptom scales: the global health quality of life, the functional quality of life, and the symptomatic quality of life (9). Two questions assess global health status. The items of functional scale include physical, role, emotional, cognitive, and social functioning. The symptom scale includes the following items: fatigue, nausea and vomiting, pain, dyspnoea, insomnia, loss of appetite, constipation, diarrhea, and financial problems. Each item seeks an answer on a four-point scale, 1=not at all, 4=very much, except for the two global health/QoL items, where questions need an answer on a seven-point scale, where 1=very poor, 7=excellent. Higher scores on the functional and global health scales represent a high QoL, whereas higher scores on the symptom scale represent a high level of symptomatology and problems. We calculated QoL scores according to the EORTC scoring manual (10). There are no standard principles concerning the construction and use of sum scores (11). Thus, we determined the mean sum scores of the scales; the functioning score, the symptoms score, and the global score.

We used a 3-day food record to assess energy and nutrient intake. We recorded nutrient intake for three non-consecutive days, including one day during the weekend, which is one of the generally accepted test methods for a nutrition consumption, based on the National Population Health Survey 2003 sample (12,13). Nutrient intake was estimated using the NutriComp Étrend Sport 3.0 software. A nutrition specialist performed the instructions for filling the form, validation,

and evaluation of nutrition diaries. Food records show general daily food intake. Because of the side effects of chemotherapy, e.g., loss appetite, nausea, and vomiting, patients receiving chemotherapy started recording their daily food intake on the fifth or seventh day after chemotherapeutic treatment. We compared the data of the energy ratio of the macronutrients and fiber intake with the recommended values of the national nutrition data table (14). During the evaluation of energy and protein intake, we also took the European Society for Clinical Nutrition and Metabolism (ESPEN) recommendation for cancer patients into consideration (2). There is no specific recommendation about vitamins and minerals for cancer patients (2). We also evaluated the vitamin and mineral intakes and compared them with the RDA values of the European Committee (COMMISSION DIRECTIVE 2008/100/EC) (15).

We set the statistical significance at $p<0.05$. For statistical calculations, we used the Wilcoxon rank-sum test, Fisher's exact test, and Kruskal-Wallis test.

Results

The average age of the patients in our study was 57±12.7 years (mean±SD). According to the BMI, 5% of the patients were underweight (BMI<18.5 kg/m^2), 28% of the patients were normal-weight (BMI 18.5-24.9 kg/m^2), 35% of the patients were overweight (BMI 25.0-29.9 kg/m^2) and 32% of the patients were obese (BMI≥30 kg/m^2). The average BMI was 27.4±6.2 kg/m^2. The average waist circumference of the patients was 98±15 cm. In our study, we have examined whether BMI was different in the different disease groups, and statistically, a significant difference was found ($p<0.001$). The median BMI was 25.3±4.6 kg/m^2 in patients with cervical cancer, 31.8±7.7 kg/m^2 in patients with endometrial cancer, and 27±5.6 kg/m^2 in patients with ovarian cancer. Furthermore, the average waist circumference was also investigated and found to be significant ($p<0.001$). Similarly to BMI, we found the lowest value in patients with cervical cancer (92.6±12.4 cm), a higher value was measured in ovarian cancer patients (97.4±13.8 cm) while we found the highest waist circumference in patients with endometrial cancer (107±16.4 cm).

Based on the results of the MUST screening (n=195), 46% of the gynecological cancer patients had a low risk for malnutrition (MUST score=0), 8% had medium risk (MUST score=1), and 46% had a high risk for malnutrition (MUST score= 2 or more). 7% of the patients had a BMI<20 (BMI score ≥1), 36% had the risk of inadequate nutrition intake due to 'acute disease effect' (score =2), and 33% of the patients had more than 5 % undesired weight loss in the past 3-6 months (weight loss score ≥1). Eighteen percent of the patients were affected by more than 10% unplanned weight loss. Based on the results of the MUST screening, two groups have been created in order to simplify the statistical analysis; i.) group affected by the risk of malnutrition; MUST point one or more if the risk of malnutrition is medium (8% of the patients) or high (46% of the patients), ii.) no risk of malnutrition group: MUST point was 0 (46% of the patients). The risk of malnutrition significantly differed among patients having an early or advanced stage of the tumor ($p=0.029$). Forty-two percent of the patients in early-stage and 59% of advanced-stage patients were affected by the risk of malnutrition (MUST is 1 point or more). The risk of malnutrition was also significantly different ($p<0.001$) among patients in different stages of the disease. Thirty-nine percent of the patients at the time of diagnosis, 65% of the patients under primary treatment, and 69% of the patients at the time of tumor recurrence were affected by the risk of malnutrition. The odds of malnutrition risk are 68% lower in patients at the time of diagnosis compared to those patients that are under treatment (OR= 0.32). Based on the MUST screening, no significant difference ($p=0.077$) was found based on the type of cancer. However, the risk of malnutrition was the highest in patients with ovarian cancer (62%), and it was somewhat lower in patients with cervical cancer (49%) and endometrial cancer (42.5%). Although the risk of malnutrition is significantly higher in underweight and normal-weight patients (66%) compared to overweight and obese patients ($p=0.023$), malnutrition risk is also high among overweight and obese patients (48%).

According to the results of the food record analysis (n=195), the mean energy intake was 1711±428 kcal/day or 25±9 **kcal/kg,** meaning kcal/kg of the body weight. The average protein intake was 0.99±0.3 g/kg

bodyweight indicating that 56% of the patients consumed less protein than 1 g/kg body weight. Macronutrient intake, expressed as a percentage of total energy, was 16±2% for proteins, 37±6.5% for fats, and 47±6% for carbohydrates. Most cases did not reach the recommended mineral intake. The average daily intake of calcium (Ca) and magnesium (Mg) was 60% and 76% of the recommendation, respectively. Similarly, the intake of most vitamins was also insufficient. The average intake of folate and vitamin D were 58% and 40% of the recommendation, respectively. Among important antioxidant vitamins, only the average vitamin C intake was higher than the recommended dose.-

The nutrient intake did not differ significantly among patients in the early or advanced stages of cancer. Furthermore, there were no significant differences regarding the nutrient intake at the time of diagnosis, under primary treatment or tumor recurrence, except for vitamin C (p=0.0325); the value of average intake increased with the progression of the disease and its treatment. Table 1. shows the average nutrient intake in gynecological cancer patients with the recommend-

Table 1. The average nutrient intake among gynecological cancer patients, with the recommended value

Variables	All patients	Rec. value	Patients before treat.	Patients during primary treat.	Patients during tumor rec.	p-value[a]	Early-stage	Adv. stage	p-value[b]
	N=195		*N=92*	*N=54*	*N=49*		*N=60*	*N=135*	
	100%		*47%*	*28%*	*25%*		*31%*	*69%*	
Energy (Kcal)	1711.4	-	1774.9	1652.1	1657.7	0.0875	1697	1718	0.9737
Protein (g)	67.4	-	69.2	65.8	65.8	0.2596	67.9	67.2	0.7167
Protein (E%)	15.9	10-15	15.8	16.1	16.1	0.3997	16	16	0.7686
Fat (g)	69.9	-	72.8	66.3	68.4	0.1976	67.8	70.9	0.6285
Fat (E%)	36.8	≤ 30	36.8	36.3	37.2	0.5113	36	37	0.4317
Carbohydrate (g)	199.5	-	206.8	194.4	191.1	0.1301	200.2	199.1	0.5111
Carbohydrate (E%)	46.9	55-60	46.9	47.3	46.3	0.4613	47.5	46.6	0.7311
Fiber (g)	18.2	20-25	18.1	18.2	18.4	0.9472	18.2	18.2	0.5435
Calcium (mg)	484.4	800	484.9	462.7	507.2	0.5699	499	478	0.3585
Magnesium (mg)	284.2	375	282.5	288.4	282.8	0.8822	282	285	0.6285
Iron (mg)	7.9	14	7.9	7.9	8	0.9573	7.7	8	0.9146
Copper (mg)	0.7	1	0.7	0.7	0.7	0.8310	0.7	0.7	0.9190
Zinc (mg)	6.4	10	6.7	6.3	6.3	0.2089	6.3	6.5	0.7249
Manganese (mg)	1.7	2	1.5	2.2	1.6	0.9210	1.4	1.9	0.4747
Chromium (μg)	41.5	40	40.9	41.8	42.3	0.9742	41.4	41.5	0.8131
Vitamin A (μg)	414.1	800	405.7	439.6	401.9	0.7800	476	387	0.4713
Vitamin B1 (μg)	791.3	1100	796.4	795.9	776.5	0.5958	782	795	0.8388
Vitamin B2 (μg)	938.1	1400	955.3	911.3	935.4	0.5352	938	938	0.6580
Vitamin B6 (μg)	1472.6	1400	1469.8	1529.8	1414.7	0.8923	1480	1469	0.9299
Vitamin B12 (μg)	2.1	2.5	2.2	1.9	1.9	0.1486	2	2	0.6660
Vitamin C (mg)	138	80	101.9	143.2	200.2	0.0325	143	136	0.8067
Vitamin D (μg)	2.1	5	2.1	1.9	2.3	0.9018	2	2	0.9124
Vitamin E (mg)	11.1	12	10.8	11.1	11.8	0.8316	11	11	0.5637
Folate (μg)	116.1	200	110.5	114.9	128.2	0.5790	112	118	0.8668

Abbreviations: Adv.stage, Advanced stage; E%, percent of total energy; Patients before treat., Patients before treatment; Patients during primary treat., Patients during primary treatment; Patients during tumor rec., Patients during tumor recurrence; Rec.value, Recommended value. (a) The Kruskal-Wallis test evaluated the statistical calculation. (b) The Wilcoxon rank-sum test evaluated the statistical calculation

ed values. Furthermore, it is of note that nutrient intake was not significantly different when underweight and normal-weight patients were compared to overweight and obese patients.

The study subjects also recorded dietary supplements in the food diary. Thirty-three percent of gynecological cancer patients consumed some dietary supplements daily (19% of the patients at the time of diagnosis, 54% of the patients under primary treatment, and 35% of the patients at the time of tumor recurrence), most commonly vitamin C.

We evaluated the data of the EORTC-QLQ-C30 survey in order to assess the quality of life. The main scales of quality of life and their shifts were investigated among patients before treatment, during primary treatment and treatment of tumor recurrence. Furthermore, we also investigated whether malnutrition risk affects the quality of life. The evaluation of functional, symptomatic and global QoL in all groups, was found to be the most valued at the time of diagnosis, before any therapeutic interventions, it turned out to be worse during the primary treatment, and it was the worst in patients with tumor recurrence. Higher scores in the functional and global health scales represent a better QoL, whereas higher scores on the symptom scales represent a high level of symptomatology and other complications. Based on our findings, the quality of life is strongly related to malnutrition risk. Patients affected with the risk of malnutrition, represented by one or more MUST points, also showed significantly worse functional, symptomatic, and global QoL compared to patients without malnutrition risk, represented by 0 MUST point. Table 2. shows the QoL among patients, before treatment, during primary treatment and at tumor recurrence, and among patients without (MUST score 0) and with the risk of malnutrition (MUST score one or more).

Discussion

Our results showed that the average BMI was 27.4 kg/m^2, 67% of the gynecological cancer patients were overweight and obese according to the BMI, and the average waist circumference was 98 cm. Data in the literature suggests that waist circumference higher than 88 cm substantially increases the risk of metabolic complications and represents abdominal obesity (7). These values were the highest in patients with endometrial cancer, which are known to be risk factors for the disease (16). Several mechanisms explain the link between obesity and endometrial cancer, including endogenous sex steroid hormones, insulin resistance, and inflammation. Abdominal fat may be biologically different from fat in other areas. Metabolically active visceral fat releases growth factors, inflammatory markers, free fatty acids, estrogen, and adipokines. All of these might contribute to the development of cancer (6,16). Based on the results of the MUST screening, there is a high risk of malnutrition. Overall, 54% of patients

Table 2. Mean scores for QoL among patients, and among patients without (MUST score 0) or with (MUST score one or more) malnutrition risk

QoL scales	All patients	Cron-bach's α	Patients before treat.	Patients during primary treatment.	Patients during tumor rec.	p-value[a]	No risk*	At risk*	p-value[b]
	N=195		*N=92*	*N=54*	*N=49*		*N=90*	*N=105*	
	100%		*47%*	*28%*	*25%*		*46%*	*54%*	
Function (15item)	74	0.881	77	75	66	0.02	79	69	<0.001
Symptom (13item)	27	0.869	22	29	36	<0.001	21	33	<0.001
Global (2 item)	54	0.857	59	56	43	<0.001	59	50	0.001

Abbreviations: MUST, Malnutrition Universal Screening Tool; Patients before treat., Patients before treatment; Patients during primary treat., Patients during primary treatment; Patients during tumor rec., Patients during tumor recurrence; QoL, Quality of life. *Risk of malnutrition assessed using the MUST; (a) The Kruskal-Wallis test evaluated the statistical calculation. (b) The Wilcoxon rank-sum test evaluated the statistical calculation

with gynecological cancer were affected by the risk of malnutrition. 39% of patients were affected at the time of diagnosis, and this rate is considerably higher during the treatment. Eighteen percent of the patients suffered from more than 10% undesired weight loss. It suggest poor prognosis (17). In many cases, the resting energy expenditure can be increased, leading to weight loss with reduced food intake. Also, the tumorous host is characterized by increased catabolism in both muscle and adipose tissue. Often inherent insulin resistance, increased fat, and protein degradation, thereby reducing fat store, as well as muscle mass. These are accompanied by elevated levels of inflammatory cytokines, which directly affect the appetite. All of these contribute to weight loss (4,17).

The nutrient intake did not differ significantly between patients in the early or advanced disease stage. It is perhaps due to that despite the disease, the patients consciously try to maintain healthy eating habits. Furthermore, except vitamin C intake that increased during the treatment, no significant difference was detected regarding the nutrient intake between patients at the time of diagnosis, during primary treatment, and at the time of tumor recurrence. The reason for higher vitamin C intake might be the frequent use of vitamin C supplements also recorded in the food records.

The ESPEN guideline recommends ≥1 g/kg/day protein intake for cancer patients, and a target dose is 1.2–2 g/kg/day, while the recommended energy intake is generally between 25 and 30 kcal/kg/day (2). Our results show that the average energy and protein intake was 25 kcal/kg and 0.99 g/kg, respectively. This also suggest, that achieving these targets can be difficult in many cases, which can be explained by decreased food consumption due to among other things, decreased appetite, early satiety, nausea. These results support previous observations in various cancer patients (18,19,20). Furthermore, based on our survey, the intake of most vitamins and minerals were less than the recommended range in Hungarian gynecological cancer patients. Data in the literature suggest that micronutrients might function as antioxidants and anti-mutagens, indicating that micronutrient deficiencies can lead to several cellular dysfunctions, including DNA damage and cancerous mutations (21). Sufficient micronutrient supply is essential in wound healing and proper functioning of the immune system, which is particularly important in cancer. The absence of micronutrients is related to specific symptoms. Nutritional deficiencies and insufficient nutritional status, malnutrition affect many cancer patients. It also harms antineoplastic treatment, prognosis, and quality of life (22).

Based on our study, malnutrition risk is prevalent in gynecological cancer patients. We found a strong correlation between malnutrition risk and quality of life. It is in agreement with previous studies which have also reported that malnutrition is common, and a significant issue in gynecologic oncology patients (23-25), and insufficient nutritional status harms the quality of life (23,26).

According to our best knowledge, this was the first detailed nutrition survey among Hungarian gynecological cancer patients. However, this study has some limitations. The limited size of our study population makes it impossible to generalize our conclusions to a larger population. It is also of note that the 3-day food record used in this study has some limitations. The reliability of food records is often questionable due to fatigue of the responders. If study subjects do not record meals immediately after consumption, they might forget to record all the food that they took. Another issue is underreporting; overweight and obese patients frequently deny their food intake resulting in debatable accuracy and reliability of this investigation (12).

Our study adds to findings of previous reports that early detection of the risk of malnutrition and nutritional deficiencies during anticancer therapies is essential in order to decrease the prevalence of malnutrition and increase the success of therapeutic interventions. Malnourishment is common in several patients at the time of diagnosis, and the side effects of cancer treatments further deteriorate the nutritional status of the patients. Nutritional interventions, food service (e.g., menu and service modification, addition of food and oral nutrition supplements, or enhanced eating environments) may improve clinical outcomes. Thus, dietitians play an essential role in the treatment of malnutrition during tumor therapies (27,28). Regular assessment of the nutritional status of cancer patients and the early detection of eating disorders are essential. Nutritional therapy should be started as early as

possible in patients identified with a high risk of malnutrition in order to maintain or improve their nutritional status. Inaccurate treatment of eating problems can contribute to the limitations of anticancer therapy. It is also essential to expand the patients' knowledge of nutrition. Nutrition counseling and the use of dietary supplements can stabilize the bodyweight and might provide improvement in nutrient intake and quality of life. Both the individualized diet and diet control are required (2).

These findings indicate the need for further, more detailed nutritional studies among gynecological cancer patients.

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