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Original Research

Nutritional assessment among patients with cervical cancer and controls

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Summary

The present study aims to acquire an insight into the nutrition of cervical cancer patients, to assess food consumption pattern in patients and controls, to identify assess dietary deficiencies in women recently diagnosed with cervical cancer compared to controls, and to investigate dietary changes during treatment. This study was conducted among 65 patients diagnosed with cervical cancer, and 170 controls, at the Division of Gynecological Oncology of the University of Debrecen, in Hungary. The authors used the food frequency questionnaire and the three-day diet record to assess nutrition. Based on the results, the consumption frequency of vegetables and legumes was significantly lower among the cases. Patients' dietary intake of vitamin D, C, and folate was significantly lower at the time of diagnosis, compared to controls. Nutrient intake is similarly insufficient among patients during the treatment. The present results show nutritional problems among cervical cancer patients and further research is required.

Key words: Cervical cancer; Nutrition survey; Nutrient intake; Food consumption.

Introduction

The number of malignant cancers is rising. The cervical cancer is the fourth (with 528,000 new cases diagnosed worldwide in 2012) most common cancer in women and it caused an estimated 266,000 number of deaths worldwide in 2012, therefore it definitely an important public health problem [1]. Cervical cancer is presumed to have a cofactorial etiology, with the well-known the infection of HPV as the major risk factor, but it is also a non-sufficient cause of cervical cancer because several other factors are also associated, interacts with other cofactors, including nutritional ones, which influence the progression [2-4]. Oxidative stress is considered to be involved in the pathogenesis of cervical cancer, so antioxidant deficiency can be an important promoting factor in cervical carcinogenesis [3]. Based on previous studies it is presumable that folate, retinol, and vitamin E probably have a protective effect, while this effect is possible for vegetables, vitamins C and B12, alpha-carotene, and beta-carotene, in relation cervical dysplasia [2].

Nutrition does not receive enough attention in the risk of cervical cancer and during treatment. There are limited studies conducted on the relationship between diet and cervical cancer and the findings are inconsistent, so there is need for more research on nutrition before and during treatment. In order to be able to formulate suggestions, either for prevention or for treatment period, it is important to know the patients' nutritional habits, and to discover possible deficiencies or nutritional problems. The aim of this study was to assess food consumption pattern in cervical carcinoma patients and controls, to identify assess dietary deficiencies in women recently diagnosed with cervical cancer compared to controls, and to investigate the differences of the nutrient intake between patients under treatment and patients at the time of diagnosis.

Materials and Methods

The study subjects included 65 female adult patients (≥ 18-years-old) diagnosed with cervical cancer, who were compared with 170 female controls. The controls were selected at random and appeared in the different departments of the same clinic. The control group did not include women with malignant disease, and they do not follow a special or different nutrition from the traditional diet. During the study, 34% patients had early and 66% had advanced-stage of cancer. The survey was created during the time of diagnosis-before any therapeutic intervention, in case of 54% of the patients, and during treatment, including chemotherapy and/or radiation therapy at 46%. This study was conducted at the University of Debrecen, Faculty of Medicine, Department of Obstetrics and Gynecology, Division of Gynecological Oncology, in Hungary, between 2016 and 2018. The ethics commission approved the study protocol (ETT-TUKEB license: 18424-2/2016/EKU 0430/16).

The authors used a questionnaire to identify risk factors, which included information about sociodemographic factors, gynecology history (including family history of gynecological cancer, parity, use of oral contraceptive), consumption of dietary supplements, anthropometric characteristics (height, weight), which were measured when the questionnaire was presented. BMI was

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Table 1. — *Frequency of various food consumption in cervical cancer cases and controls.*

Frequency of food consumption			Cases (n = 65)	Controls (n = 170)	*p*-value
Milk	Low-fat	Frequent	46%	47%	1.000
		Rare	54%	53%	
	Fatty	Frequent	40%	43.5%	0.660
		Rare	60%	56.5%	
Sour cream	Low-fat	Frequent	34%	38%	0.550
		Rare	66%	62%	
	Fatty	Frequent	51%	56.5%	0.466
		Rare	49%	43.5%	
Cheese	Low-fat	Frequent	26%	24%	0.738
		Rare	74%	76%	
	Fatty	Frequent	69%	70%	1.000
		Rare	31%	30%	
	Processed (cube cheese)	Frequent	49%	39%	0.183
		Rare	51%	61%	
Kefir, yogurt		Frequent	75%	74%	1.000
		Rare	25%	26%	
Eggs		Frequent	91%	93%	0.588
		Rare	9%	7%	
Pork	Low-fat	Frequent	71%	71%	1.000
		Rare	29%	29%	
	Fatty	Frequent	45%	39%	0.553
		Rare	55%	61%	
Poultry meat	Chicken, turkey-without	Frequent	74%	66.5%	0.346
	Skin	Rare	26%	33.5%	
	Chicken, turkey-with skin,	Frequent	48%	39%	0.238
	Duck, goose	Rare	52%	61%	
Beef		Frequent	14%	10%	0.485
		Rare	86%	90%	
Fish, canned fish		Frequent	38.5%	49%	0.146
		Rare	61.5%	51%	
Offals	Liver, kidney	Frequent	18.5%	17%	0.848
		Rare	81.5%	83%	
Cold cuts	Frankfurter	Frequent	57%	55%	0.884
		Rare	43%	45%	
	Ham	Frequent	66%	57%	0.236
		Rare	34%	43%	
	Salami	Frequent	46%	42%	0.559
		Rare	54%	58%	
Smoked goods		Frequent	45%	41%	0.658
		Rare	55%	59%	
Bacon, greaves		Frequent	45%	41%	0.658
		Rare	55%	59%	
To spread on bread	Butter	Frequent	37%	28%	0.209
		Rare	63%	72%	
	Margarine	Frequent	74%	79%	0.485
		Rare	26%	21%	
	Fat	Frequent	29%	24%	0.504
		Rare	71%	76%	
Oil seeds	Walnut, peanut,	Frequent	66%	73.5%	0.264
	pumpkin seed	Rare	34%	26.5%	
“Fast foods”	Hamburger, hot dog	Frequent	12%	6.5%	0.180
		Rare	88%	93.5%	
Muesli, cereal-flakes	Natural	Frequent	38.5%	39%	1.000
		Rare	61.5%	61%	
	Flavored	Frequent	28%	25%	0.621
		Rare	72%	75%	
White bread, bakery products		Frequent	71%	77%	0.316
		Rare	29%	23%	

Brown bread, bakery products		Frequent	60%	52%	0.309
		Rare	40%	48%	
Whole wheat bread, bakery products		Frequent	48%	49%	0.885
		Rare	52%	51%	
Cooked pasta	Noodles, macaroni,	Frequent	78.5%	80%	0.857
	spaghetti	Rare	21.5%	20%	
Baked noodles, cake	Pancakes, cake, strudel	Frequent	63%	63%	1.000
		Rare	37%	37%	
Potato	pottage, masked potatoes,	Frequent	91%	94%	0.390
	cooked potatoes	Rare	9%	6%	
	fried potatoes in fat	Frequent	52%	55%	0.771
		Rare	48%	45%	
Rice		Frequent	83%	86%	0.682
		Rare	17%	14%	
Dry legumes	Beans, yellow peas, lens	Frequent	48%	62%	0.054
		Rare	52%	38%	
Soy, soy products		Frequent	6%	3.5%	0.470
		Rare	94%	96.5%	
Green pottage		Frequent	59%	66%	0.293
		Rare	41%	34%	
Vegetables	Paprika, tomatoes,	Frequent	94%	99.4%	0.022
	cucumber, raw salads..	Rare	6%	0.6%	
Pickles	Cucumber, mixed pickles,	Frequent	92%	94%	0.566
	beets..	Rare	8%	6%	
Fruits	Apple, pear, banana,	Frequent	100%	100%	
	lemon..	Rare	0%	0%	
Compote, jam		Frequent	68%	68%	1.000
		Rare	32%	32%	
Juice	Fibrous and fresh	Frequent	72%	68%	0.532
		Rare	28%	32%	
Soft drink	Carbonated soft drink,	Frequent	35%	42%	0.457
	filtered juice, syrup	Rare	65%	58%	
Tap water		Frequent	69%	73%	0.627
		Rare	31%	27%	
Mineral water		Frequent	88%	80%	0.188
		Rare	12%	20%	
Tea		Frequent	80%	83%	0.575
		Rare	20%	17%	
Coffee		Frequent	81.5%	71%	0.134
		Rare	18.5%	29%	
Sweets: candy, chocolate, cookies..		Frequent	72%	71%	0.873
		Rare	28%	29%	
Ice cream		Frequent	41.5%	35%	0.450
		Rare	58.5%	65%	

derived from a weight/height^2 ratio and the authors assessed it according to the WHO classifications [5]. They measured waist circumference too, besides the BMI, which is a simple method for the assessment judgement of central obesity. The measurement was carried out halfway between the top of the hip blade and the lower rib edge [6]. The food frequency questionnaire was used to obtain information regarding their food consumption pattern. The consumption frequency questionnaire provides information on the consumption patterns of a larger period of time and it can provide information about the connection between specific food and diseases [7]. The study subjects were asked to indicate the average frequency of consumption of the last one year. The FFQ included 39 main food and beverage categories, which the most common ones in the diet. The frequency of food consumption was as follows: several times a day, daily, 1-3 times a week, and 1-3 times a month were coded frequent; furthermore less frequently than one month and not consumed, were coded rare. The authors used the three-day diet record to gather information on different nutritional variables, such as caloric intake, fats, protein, carbohydrates, cholesterol, fiber intake, vitamins and minerals among cervical cancer patients and controls, detailing nutrient intake for three non-consecutive weekdays, including one weekend day, which is one of the generally accepted test methods for a nutrition consumption, based on National Population Health Survey 2003 sample [7, 8]. After detailed information, a nutritional specialist instructed the patients to complete the record in their home. They also recorded the supplements in their dietary diary. At the next meeting, when they returned the record, the nutritional specialist checked the validity of the responses, interviewed the patients to check for incomplete recordings, preparation procedures, and consumed quantities. Nutrient intakes were estimated by using the NutriComp Étrend Sport 3.0 software, by a nutritional specialist.

In terms of nutrition intake, and controls were compared only with the patients at the time of diagnosis, as the dietary habits could have changed during treatment, the patients undergoing treatment, were compared separately to patients before treatment, that are at the time of diagnosis. During assessing of nutrient intake (including macronutrients, retinol equivalents), the authors took into account the national nutrition data table [9], and the results for the intake of vitamins and minerals were compared with the Recommended Dietary Allowance (RDA), as presented by the European Commission Directive 2008/100/EC [10]. Statistical significance was achieved when $p < 0.05$. Statistical significance was evaluated by Wilcoxon rank-sum (Mann-Whitney) test and Fisher's exact test.

Results

There was no significant difference between patients (n = 65) and controls (n = 170) with aspect to age (p = 0.0906), education (p = 0.266), settlement (p = 0.686), parity (p = 0.759), age at first birth (p = 0.5318), marital status (p = 0.968). Although not significant, the use of oral contraceptives was more common in patients (p = 0.436) and used for an extended period (p = 0.9954), compared to controls. Seventy-two percent of patients consumed oral contraceptives for nine years on average, while 66% of controls, for seven years. Twenty-five percent of patients had gynecological tumor in their family histories, significantly higher (p = 0.034) than in controls (12%), while 8% of cases and 11% of controls did not know it.

No significant differences were observed between cases and controls for BMI and waist circumference, but in both cases, among patients and controls, it was higher than the ideal value. The average BMI was 25.3 kg/m^2 in patients, and 26 kg/m^2 in controls (p = 0.0611), which can be classified as overweight based on BMI category. The average of waist circumference was 92.6 cm in patients, and 91.4 cm in controls (p = 0.3911), which presents abdominal obesity.

The food consumption frequency did not differ between cases (n = 65) and controls (n = 170), except for the consumption of vegetables (p = 0.022), and legumes (p = 0.054). Among the cases, their consumption was more common. Among the patient subjects 51%, while 64% among controls consumed vegetables daily or several times a day, 26% of cases, 30% of controls 1-3 times a week, while a high rate of cases, 17% consumed only 1-3 times a month and 6% less frequently than one month. Legumes are consumed 1-3 times a week in 14.7% of the controls and 12.3% of the cases, 1-3 times a month 47.6% of controls and 35.4% of the cases, while consumed less frequently than one month 31.8% and not consumed 5.9% of controls, 43.1% and 9.2% of cases. The non-significant results are not detailed separately. The results of food frequency consumption are summarized in Table 1.

Based on the results of nutrition diaries, compared with controls, patients at the time of diagnosis (n = 35) had significantly higher protein intakes, within that animal protein (p = 0.0074), but the energy, total and specific fats, cholesterol, carbohydrate and dietary fiber intake did not differ significantly. Considering nutrient ratios, there was no significant difference among cases and controls, but the fat energy exceeded the upper limit of the recommen-

Table 2. — *The average macronutrients intake among patients before treatment and controls.*

	Controls (n = 170)	Patients before treatment (n = 35)	*p*-value
Energy (kcal)	1 764.18	1 787.25	0.8979
Protein (grams)	66.35	70.57	0.0600
Animal protein (grams)	36.04	41.36	0.0074
Vegetable protein (grams)	30.23	29.21	0.2457
Fat (grams)	69.63	69.11	0.7425
Animal fat (grams)	35.25	37.34	0.7567
Vegetable fat (grams)	34.38	31.77	0.1920
MUFA (grams)	21.51	21.15	0.4932
PUFA (grams)	17.53	17.55	0.9153
SFA (grams)	19.66	20.12	0.8658
Cholesterol (mg)	261.95	291.66	0.1984
CHO (grams)	214.25	217.06	0.8732
Dietary fiber (grams)	20.44	18.77	0.1610
% Energy from Protein	15.13	15.96	0.0935
% Energy from Fat	35.49	34.76	0.4775
% Energy from SFA	10.01	10.10	0.8218
% Energy from MUFA	10.97	10.64	0.4195
% Energy from PUFA	8.98	8.82	0.6210
% Energy from CHO	49.00	48.94	0.6388

MUFA: monosaturated fatty acids; PUFA: polysaturated fatty acids; SFA: saturated fatty acids; CHO: carbohydrates.

Table 3. — *The average micronutrients intake-with RDA among patients before treatment and controls.*

	EU RDA	Controls (n=170)	Patients before treatment (n=35)	*p*-value
Ca (mg)	800	518.36	506.82	0.8535
Mg (mg)	375	313.94	294.80	0.3447
Fe (mg)	14	8.27	8.01	0.4932
Cu (mg)	1	0.79	0.76	0.5459
Zn (mg)	10	6.40	6.64	0.1984
Mn (mg)	2	1.50	1.59	0.6478
Cr (μg)	40	43.67	40.98	0.1307
Vitamin A (μg)	800	491.92	328.42	0.1826
RE (mg)	0,8	0.74	0.58	0.1676
Vitamin B1 (μg)	1100	812.61	770.01	0.7591
Vitamin B2 (μg)	1400	911.17	935.57	0.5840
Vitamin B6 (μg)	1400	1 596.91	1 518.60	0.5274
Vitamin B12 (μg)	2.5	2.11	2.07	0.4322
Vitamin C (mg)	80	148.95	83.86	0.0113
Vitamin D (μg)	5	4.00	1.81	0.0336
Vitamin E (mg)	12	12.13	11.13	0.1051
Niacin (mg)	16	11.40	12.63	0.1857
Folate (μg)	200	115.32	101.45	0.0487
Biotin (μg)	50	22.98	20.84	0.2062
Pantothenic acid (mg)	6	2.82	2.85	0.8462

Ca: calcium; Mg: magnesium; Fe: iron; Cu: copper; Zn: zinc; Mn: manganese; Cr: chromium; RE: retinol equivalent.

Table 4. — *The average macro- and micronutrients' intake among patients before treatment and patients undergoing treatment.*

	Patients before treatment (n=35)	Patients undergoing treatment (n=30)	*p*-value
Energy (kcal)	1,787.25	1,747.86	0.2018
Protein (grams)	70.57	66.28	0.1671
Animal protein (grams)	41.36	36.67	0.7422
Vegetable protein (grams)	29.21	29.54	0.0617
Fat (grams)	69.11	69.09	0.7125
Animal fat (grams)	37.34	35.53	0.9266
Vegetable fat (grams)	31.77	33.56	0.4221
MUFA (grams)	21.15	21.53	0.7027
PUFA (grams)	17.55	17.34	0.3924
SFA (grams)	20.12	19.58	0.7422
Cholesterol (mg)	291.66	268.82	0.7224
CHO (grams)	217.06	211.54	0.0947
Dietary fiber (grams)	18.77	19.92	0.1972
% Energy from Protein	15.96	15.27	0.4938
% Energy from Fat	34.76	35.58	0.5276
% Energy from SFA	10.10	10.08	0.4221
% Energy from MUFA	10.64	11.09	0.0896
% Energy from PUFA	8.82	8.97	0.9580
% Energy from CHO	48.94	48.77	0.6451
Ca (mg)	506.82	505.02	0.0801
Mg (mg)	294.80	305.46	0.1084
Fe (mg)	8.01	8.19	0.5537
Cu (mg)	0.76	0.77	0.2415
Zn (mg)	6.64	6.31	0.0353
Mn (mg)	1.59	1.49	0.4221
Cr (µg)	40.98	43.35	0.7823
Vitamin A (µg)	328.42	511.57	0.2210
RE(mg)	0.58	0.75	0.8642
Vitamin B1 (µg)	770.01	800.33	0.2865
Vitamin B2 (µg)	935.57	908.72	0.5450
Vitamin B6 (µg)	1 518.60	1 562.85	0.3709
Vitamin B12 (µg)	2.07	2.11	0.3173
Vitamin C (mg)	83.86	149.80	0.1591
Vitamin D (µg)	1.81	3.71	0.1055
Vitamin E (mg)	11.13	11.90	0.6170
Niacin (mg)	12.63	11.37	0.3709
Folate (µg)	101.45	114.46	0.4453
Biotin (µg)	20.84	22.80	0.5805
Pantothenic acid (mg)	2.85	2.82	0.6357

MUFA: monosaturated fatty acids; PUFA: polyunsaturated fatty acids; SFA: saturated fatty acids; CHO: carbohydrates; Ca: calcium; Mg: magnesium; Fe: iron; Cu: copper; Zn: Zinc; Mn: manganese; Cr: chromium; RE: retinol equivalent.

dation (< 30 E%), the average protein E% was slightly higher than recommended (10-15 E%), exactly in cases, while the carbohydrate ratio was below the recommendation (55-60 E%). Fiber intake, although not significant, however was higher in controls, and unfortunately, it was below the recommended value (20-25 g/d) among the patients. Table 2 presents the macronutrients intake among patients before treatment (who are at the time of diagnosis) and controls. Vitamin D ($p = 0.0336$), furthermore vitamin C ($p = 0.0113$), and folate intake ($p = 0.0487$) were significantly higher in the controls. Although not significant, controls had slightly higher mean intakes of micronutrients, such as calcium, magnesium, vitamin A, retinol equivalents (RE), and vitamin E. Overall, the median intakes of micronutrients were below the recommended in both. Table 3 presents the micronutrients intake-with RDA, among patients before treatment and controls. The consumption rate of dietary supplements did not differ between patients at the time of diagnosis and controls on a daily basis and 14% of patients and 14% of controls were consuming supplements, and the most common was vitamin C.

The authors examined the difference in the nutrient intake between patients at the time of diagnosis (n = 35) and patients undergoing treatment (n = 30), and they di not find a significant difference between nutrient intake values, except the zinc intake, which was lower among patients who were undergoing treatment, although some micronutrients intake, such as vitamin C, D, A, retinol equivalent, and folic acid intake were somewhat higher, albeit not significant and were still lower than the recommendations among them. The average protein intake was slightly lower than in patients at the time of diagnosis; expressed as body weight it was 1.09 g/kg body weight in patients at the time of diagnosis and 0.96 g/kg in patients undergoing treatment ($p = 0.6078$). Table 4 presents the macro- and micronutrients intake of patients before treatment and patients undergoing treatment. The daily intake of dietary supplements was significantly higher among patients undergoing treatment compared to patients at the time of diagnosis ($p = 0.037$), and 40% of them consumed daily supplements, and the most common was vitamin C.

Discussion

This study assessed the nutrition of cervical cancer patients, compared with controls. Based on the present results, food frequency consumption for most items was not different between cases and controls, except for vegetables and legumes, whose consumption frequency was significantly lower in cases. Earlier studies reported that vegetable consumption has a protective role against several common cancers [11, 12]. The micronutrients intake of cervical cancer patients and controls, was largely insufficient with reference to RDAs, so not specifically the patients are characterized by inadequate intake; this is probably associated with the home national dietary habits, but there are sharper deficiencies among patients, any important micronutrients intake values, such as vitamin A, E, retinol equivalents, even if not significant, was higher in controls compared to the patients at the time of diagnosis. There were significant differences in vitamin C, D, and folate intake; their intake was considerably higher among the con-

trols. So the results of nutrition diaries suggest that the intake of vitamins in women with cervical cancer is more defective, which may be related to less frequent consumption of vegetables, because these are the rich sources of vitamins that function as antioxidants [13]. Labani *et al.* studied similarly the dietary pattern among uterine cervical cancer patients and normal controls, they did not find significant differences in the food consumption profile among patients and controls, but similarly the nutrient intake was low compared to the RDA in both groups [14]. Several studies suggest that the intake of antioxidant vitamins influenced the risk of cervical cancer [15-17]. Evidence indicates that micronutrient deficiencies may contribute to DNA damage and could promote tumorigenesis; in this way dietary deficiencies can be a serious factor in cancer risk [18], furthermore, oxidative stress, can play a role in the progression and pathogenesis of cervical cancer [19], therefore insufficient consumption of vegetables - which contain high concentrations of dietary fiber, vitamins, minerals, and antioxidants [13] may be an important risk factor. The nutrient intake of patients undergoing treatment did not deviate significantly from the patients at the time of diagnosis; the intakes were deficient compared to the recommendation. Although the intake of some micronutrients was slightly higher than in patients at the time of diagnosis, presumably they are trying to pay more attention to their nutrition and this can be related to the significantly higher consumption of dietary supplements, but unfortunately even these many micronutrients did not reach the recommended values, furthermore, also the protein intake was lower than the recommended for cancer patients, although adequate protein intake is essential during cancer treatment, intake of at least 1 gram of protein per kilogram body weight has been suggested for cancer patients, and a target supply of 1.2-2 g/kg/day [20]. The diet and the proper nutritional status have an important role not only in prevention, but they may also influence the course of disease and cancer progression. After cancer diagnosis, the consumption of a nutrient-dense diet is essential to provide adequate elements for healing and a defense side effects, against a later cancer recurrence [21].

This study focused on the evaluation and comparison of nutrition due to the lack of such data. Although the number of cases may not necessarily be extrapolated to a larger population the results, and it is aimed at the population of Hungary, the present study suggests that there are significant nutritional deficiencies among cervical cancer women so further nutritional studies are justified. The adequate micronutrient intake, may be a protective factor, so it is necessary to optimize vitamin and mineral intake by encouraging dietary change, and to increase the consumption of vegetables to reduce the risk of cancer [18]; furthermore it is necessary to evaluate deficiencies during treatment, to expand women's knowledge with nutritional guidance, and to emphasize the role of nutrition for successful healing [20, 21].

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