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Original Article

Malnutrition and Risk Factors in Tunisian Patients with Colorectal Cancer

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Abstract

Background and Objectives: Colorectal cancer (CRC) is the most frequent digestive cancer. Its occurrence is associated with many factors including nutrition and lifestyle. CRC is often associated to malnutrition which worsens its prognosis. The objectives of the study were to evaluate the nutritional status of patients with CRC. **Patients and Methods:** A retrospective study about fifty patients with CRC recruited in the Department of Gastroenterology and Surgery of "La Rabta" Hospital in Tunis as well as fifty random controls. The groups were matched for age and sex. The nutritional status of patients was assessed by anthropometric measurements, laboratory tests (albumin), and three nutritional scores. Dietary intakes were quantified by a frequency questionnaire and 24-h recall. **Results:** Significant risk factors were obesity ($P = 0.02$), menopause ($P = 0.006$) and the high consumption of red meat ($P = 0.002$), processed meat ($P = 0.002$), fried foods ($P = 0.0001$), and sugar ($P = 0.0001$). The consumption of green tea ($P = 0.003$), fruit ($P = 0.001$), and cereals ($P = 0.0001$) was higher in controls. Malnutrition was common measured by the body mass index, the percentage of weight loss (42%), albumin (60%), and different nutritional scores. The energy and protein intakes of patients were below the recommended requirements in 94% and 92% of patients, respectively. Deficiencies in minerals, vitamins, and trace elements were found. **Conclusions:** Malnutrition was very common in patients with CRC with multiple vitamin and mineral deficits.

Keywords: Albumin, colorectal cancer, malnutrition, nutritional risk index

Introduction

Colorectal cancer (CRC) is a major health problem because of its increasing frequency in Tunisia.[1] Worldwide, CRC is a major public health problem by increasing prevalence, and it associated morbidity and mortality. There are over one million new cases diagnosed every year worldwide and results in half a million deaths each year representing about 8% of all cancer-related deaths.[2]

CRC is the result of a complex interaction of genetic and environmental factors; it most commonly occurs as a sporadic form and only 5% as a hereditary form.[3] Genetic susceptibility to colon cancer has been attributed both to polyposis and nonpolyposis syndromes.[2] Among nongenetic risk factors for the development of CRC, the most important are a sedentary lifestyle and obesity. In fact, proper diet (a low-fat intake and consumption of red meat and a high intake of vegetable fibers) along with frequent physical activity seems to be the best prevention tools for this malignant disease.[3-5]

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In addition to its frequent increase, CRC is also a major public health problem because of associated undernutrition in 40% of cases.[4-7] Several studies have demonstrated the pejorative effect of undernutrition on the prognosis of the cancer patient. Indeed, it is associated with higher morbidity and mortality (20% of cancer deaths occur due to this event) and is also correlated with the occurrence of multiple complications during treatments such as postoperative complications and infections.[8]

There is a lack of studies on malnutrition in Arab patients with CRC. This study aimed to evaluate the nutritional status of Tunisian patients followed for CRC and to compare their nutritional habits with a control group.

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Patients and Methods

Setting and design

This is a retrospective study of 50 cancer patients (24 men and 26 women), who are being followed up at the Department of Gastroenterology and Surgery of La Rabta Hospital in Tunis, between December 2015 and March 2016. We included patients with colon or rectum cancer or both, over 30 years of age with a positive diagnosis made by the pathological study of biopsies performed during a low digestive endoscopy. We did not include pregnant women and patients with unavailable weights or incomplete/missing medical records. Fifty controls were recruited at the same time without digestive illness and not following a diet. Patients and controls were matched for age and sex.

Nutritional assessments

Each participant has undergone a careful interrogation specifying the demographic characteristics of the patients: age, sex, sedentary lifestyle, family history, and habits (tobacco and alcohol). Biochemical assessments included plasma albumin (cellulose acetate electrophoresis), high-sensitivity C-reactive protein (CRP) (Beckman Synchron LX®20 CRP), and hemoglobin and white blood cells after the treatment for CRC. Radiological assessments included chest X-ray, abdominal ultrasound, thoracoabdominal scanner, and total colonoscopy with biopsies to determine the tumor, node, and metastasis (TNM) classification. The nutritional status of the participants, after the diagnosis and the treatment of CRC, was assessed by determining the weight, height, and calculating body mass index (BMI). BMI was considered normal ≥18.5 kg/m² and underweight if <18.5 kg/m². The waist circumference (WC) was measured, and abdominal obesity was defined by WC >80 cm in women and 94 cm in men. Brachial circumference (CB) was measured and a value <22 cm was counted to infer protein–energy malnutrition and the circumference of the calf (CM) with a value <31 cm taken as a marker of malnutrition risk.

We also specified the loss of weight in 6 months (in kg and %) (values taken from the records at the diagnosis): undernutrition – weight loss ≥5% in 1 month or ≥10% in 6 months and severe malnutrition – weight loss ≥10% in 1 month or ≥15% in 6 months. The scores we used for this same evaluation were Mini Nutritional Assessment (MNA) score, Nutritional Risk Index (NRI) score, and the Subjective Global Assessment (SGA) score. All participants benefited from an evaluation of spontaneous food consumption based on a 24-h recall questionnaire coupled with eating habits, after the diagnosis of CRC and its treatment. A food frequency questionnaire was conducted to identify nutritional risk factors. We used a food analysis program BILNUT® software (Cerelles, France) which was enriched by new components menus to assess the intake of macro- and micronutrients for patients and controls.

Statistical analysis

The statistical analysis was carried out by SPSS software: SPSS Statistics for Windows, Version 17.0. (SPSS 43 Inc. Chicago, USA) using Chi-square test for the comparison of the qualitative variables and Student's *t*-test for the comparison of the quantitative ones. The results of quantitative variables are given on mean ± standard deviation (SD). Odds ratio and relative risk were calculated. A difference is considered statistically significant if $P < 0.05$.

Results

Demographic characteristics

Fifty patients (24 men and 26 women) and 50 controls (22 men and 28 women) were matched for sex and age. The age (mean ± SD) of patients and controls was 56.1 ± 14.2 and 52.5 ± 13.2 years, respectively (not significant [NS]). Sedentary life was reported by 82% of the patients and 21% of the controls ($P = 0.003$). Menopause was reported by 22 patients and 14 controls ($P = 0.006$). There was no difference in frequency of family history of CRC (16% in each group, NS) nor smoking (16% and 9% in patients and controls, respectively, NS).

Anthropometric profile of patients

The anthropometric characteristics of the patients are summarized in Table 1. Twenty-three patients (46%) had a normal BMI and 8% of the patients had a BMI <18.5 kg/m². Mean CB was 30.7 ± 5.1 cm with only one patient counted as undernourished. The mean CM was 34.8 ± 4.4 cm. Seven patients (14%) were at risk of malnutrition by CM criteria.

Characteristics of colorectal cancer

The mean hospital stay was 2.2 ± 4.4 months. Metastases were present in 24% of patients (75% of whom were hepatic metastases). According to the TNM classification, 30% ($n = 15$) of patients had a TNM Stage 0, 28% had a TNM Stage I, and 24% had a Stage IV. Two-thirds of our patients (68%) received surgical treatment, 36% received chemotherapy, and

Table 1: Select nutritional parameters of patients at baselines and in relationship to colorectal cancer diagnosis and severity of malnutrition

Nutritional measures	Patients data and units of measurements
BMI (kg/m²)	
Before CRC	28.0±4.6
After CRC	24.6±4.7
WC (cm) after CRC diagnosis	94.7±12.3
Body weight (kg)	
Before CRC	76.8±14.6
After CRC	67.6±14.6
Weight loss	
Actual weight loss (kg)	9.3±10.7
Percentage weight loss (%)	11.7±11.0
The proportion of malnutrition, *n* (%)	21 (42)
The proportion of malnutrition, *n* (%)	14 (28)

BMI: Body mass index, CRC: Colorectal cancer, WC: Waist circumference

28% received radiation therapy. Fifteen patients have not yet received any treatment, and 36% of patients underwent surgery followed by chemotherapy sessions.

Nutritional status

Anorexia was present in all cases. The energy and macronutrient intakes are summarized in Table 2. Micronutrient and fiber intakes are summarized in Table 3 and Figure 1. The caloric intake was insufficient in 94% of patients. Protein and carbohydrate intake was insufficient in 92% and 32% of patients, respectively. The intake of monounsaturated fatty acid was insufficient in 20% of patients. Alcohol use, smoking, and physical inactivity before CRC occurred more frequently in patients than in controls, but the difference was not statistically significant. The comparison of the consumption frequency of certain foods between patients and controls is summarized [Table 4]. The average albumin level of the patients was 32.6 ± 10.8 g/L indicating undernutrition in 30 patients (60%) with an albuminemia lower than 30 g/L. Anemia was evident in 34% of men and 40% of women. The results of the various nutritional screening scores are summarized in Figure 2. Using the different nutritional screening scores (NRI, MNA, and SGA), the percentage of patients with both moderate and severe risk varied between 56% and 80%.

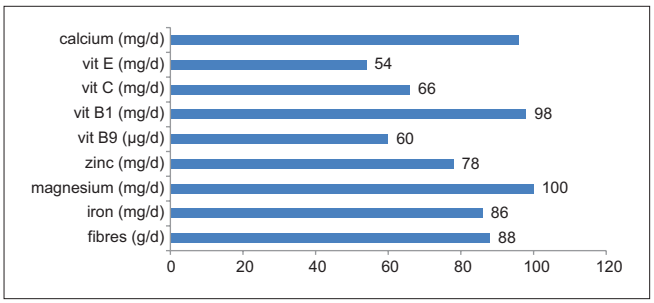

Figure 1: Percentage of patients with inadequate intake of micronutrients and fiber

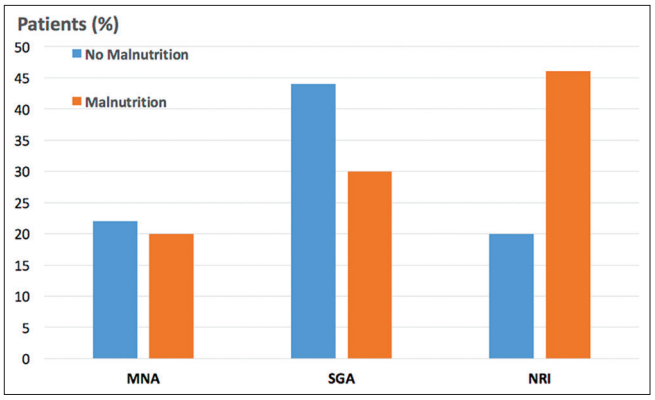

Figure 2: Evaluation of nutritional status using the different scores

Table 2: Intakes of calories and macronutrients in patients and control

Measures	Recommended nutritional intake*	Patients	Controls	Significance level
Average caloric intake (Kcal/day)	Woman: 2200; man: 2500	1262	1766	0.0001
Total carbohydrates (percentage TEI)	50-55	52.8	50.3	0.02
Sucrose (percentage TEI)	≤25	9.3	7.8	0.24
Total fats (percentage TEI)	35-40	31.5	36.4	0.002
Saturated fats (percentage TEI)	≤12	8.9	9.2	0.66
Monounsaturated fats (percentage TEI)	15-20	11.9	14.1	0.09
Polyunsaturated fats (percentage TEI)	5	10.7	13.1	0.03
Cholesterol (mg/day)	≤300	122	151	0.47
Proteins (g/kg/day)	Patients: 1.2-1.5 Controls: 0.8	0.63	0.8	0.007

*Recommended nutritional intake according to Anses 2011. TEI: Total energy intake

Table 3: Measures of intakes of micronutrients and fiber in patients and controls

Micronutrients	Recommended nutritional intake*	Patients	Controls	*P*
Fiber (g/day)	25-30	14	19	0.1
Iron (mg/day)	Woman: 9-16; man: 9	7.7	10.0	0.02
Magnesium (mg/day)	Woman: 360; man: 420	74	109	0.02
Zinc (mg/day)	Woman: 10; man: 12	7.12	7,53	0.74
Folates (µg/day)	Woman: 300; man: 330	781	590	0.27
Vitamin B1 (mg/day)	Woman: 1.1; man: 1.3	0.43	0.64	0.02
Vitamin C (mg/day)	110	111	116	0.72
Vitamin E (mg/day)	12	51	41	0.39
Calcium (mg/day)	Woman: 900-1200; man: 900	525	584	0.17
Water (ml/day)	1500	1044	1120	0.53

*Recommended nutritional intake according to Anses 2011

Table 4: The frequency of consumption of certain foods in patients and controls

Food items and meals	Patients	Controls	*P*
Fish/week	1.1	1.42	0.09
Red meat/week	2.7	1.64	0.002
Cold cuts/week	1.1	0.3	0.002
Offal-based dishes/week	1.1	0.2	0.002
Fried dishes/per week	3.0	1.8	0.0001
Milk glasses/week	4.7	4.9	0.76
Spoons of sugar/day	2.1	1.1	0.0001
Fruits/week	4.8	6.1	0.001
Vegetables/week	4.4	5.2	0.06
Cereal bowls/week	2.2	4.0	0.0001

Discussion

The mean BMI of patients was statistically lower than that before the occurrence of CRC. Only four patients had a BMI <18.5 kg/m² and were considered malnourished. Weight loss is due to a wide range of factors including decreased food intake, increased energy expenditure, loss of appetite, cancer-related treatments, and cancer-related stress itself.[9] Patients with gastrointestinal malignancies have the second highest frequency of cancer-related weight loss. People with gastrointestinal tumors lose more than 50% of their muscle mass and 30%–40% of their body fat.

In our study, the assessment of the energy intake of the patients showed an average daily energy intake below the recommendations of the energy requirements in medical oncology.[10] Several studies showed insufficient caloric intake in their populations. This contributed difference can be explained by the anorexia of the patients and the absence of nutritional care.

The various published studies showed that protein requirements are high in patients with CRC. Protein intakes between 1.2 and 1.5 g/kg/day allow to cover the estimated needs and maintain a positive nitrogen balance, compared to 0.8 g/kg/day in healthy participants. In case of an acute complication or severe malnutrition, the need is 1.5 g/kg/day.[10-16] Inadequate protein intake (<1.2 g/kg/day) was found in 92% of patients.

We found insufficient intake of calcium (96%), zinc (78%), and iron (86%). Our results are inferior to the recommendations and results observed in Sun's studies[12] and Tayyem.[13]

The average fiber intake in patients was 14.15 g/day, so 88% of the patients had inadequate intake compared to the recommendations. Our results are consistent with those of the literature. Indeed, in the recent Song study,[15] patients with CRC had an average fiber intake of 20.5 ± 8.5 g/day. This can be explained by the low intake of vegetables, fruit, and whole grains.

Our results showed that the mean albuminemia of the patients was 32.35 g/L with 60% of malnourished patients. According to Hébuterne,[16] more than half of the patients (60%) were considered to be malnourished according to the level of albuminemia. In the Sun study,[12] approximately 28.7% of patients had low albumin levels.

Using the different nutritional screening scores (NRI, MNA, and SGA), the percentage of patients with both moderate and severe risk varied between 56% and 80%. This percentage was higher than those found in the literature. Indeed, in the Tu *et al*. study on the nutritional status of 45 patients, only half of the patients were at risk of undernutrition according to the NRI.[17] Bourdel-Marchasson *et al*.[18] found that 71.7% of the cases studied presented a risk of undernutrition according to the MNA score. According to the SGA score, this percentage was 36% in Tu *et al*. study.[17]

The results obtained for NRI, MNA, or SGA can be explained by the long hospital stay, which is on average 76 days. Indeed, the risk of undernutrition increases with the length of hospital stay.[19] and also by the high number of patients operated (68%). However, we did not find significant relationships between surgery and different nutritional scores. Half of the patients consumed more than 500 g of red meat per week, which was significantly higher than controls ($P = 0.006$). A prospective Japanese study of Takashi[20] from 1995 to 2006 found that high consumption of red meat was associated with an increased risk of colon cancer, particularly among women. Mahfouz *et al*.[21] found a significant association between red meat consumption and the occurrence of CRC. This same association was found by other authors.[22,23] The World Cancer Research Fund indicated that red meat consumption increases the risk of CRC by 17% for an intake of 100 g/d and recommends a red meat consumption of fewer than 500 g/week.[24] Our patients consumed significantly more fried meals per week than controls ($P = 0.0001$). The (World Cancer Research Foundation) concluded that there was too little evidence for an increased risk of CRC in excessive consumption of fat.[25] A meta-analysis of 13 prospective studies of Liu *et al*.[26] did not reveal a significant association between dietary fat consumption and risk of CRC. Thompson *et al*.[27] showed that trans-fatty acids are suspected to increase the risk of various cancers. However, the results concerning CRC are quite divergent and do not lead to the conclusion of a definite significant association.

Our patients had a higher daily intake of sugars per day than controls. Our results are consistent with other studies[28,29] which showed that a high-sugar diet is associated with a high risk of CRC. Indeed, insulin receptors and insulin growth factor I are strongly expressed by cancerous colic cells. Insulin can thus bind to these receptors and promote their growth 1. However, according to the findings of the World Cancer Research Fund and the American Institute for Cancer Research,[30] a possible association is supported only by limited evidence. The available studies are still relatively few and lead to very discordant results. Mulholland *et al*.[31] showed

that there was no significant association between the glycemic index of foods and the risk of CRC.

We found in our study that dietary fiber intake was higher in controls than in patients. Furthermore, controls consumed significantly more cereals than patients. The inverse association between consumption of fiber (or fiber-rich food) and the risk of CRC is well established.[32-34] Park *et al*.[32] showed a 16% reduction in CRC risk by comparing the highest fiber consumption quintile (≥30 g/day) to the lowest (≤10 g/day). Murphy *et al*.[33] showed that a high-fiber diet was inversely associated with the risk of CRC and could play a preventive role against CRC. Furthermore, Aune *et al*. showed that the risk of CRC would decrease by 10% for each 10 g/day and increase in fiber consumption, a finding that fits perfectly with the systematic review of the literature.[34]

Based on our observations, patients were less likely to use fruits and vegetables with $P = 0.001$ and $P = 0.06$, respectively. In China, low consumption of green vegetables was a significant risk factor for both colon and rectal cancer. A meta-analysis carried out in 2007, involving 750,000 persons, showed no significant reduction in the risk of CRC in the case of high consumption of fruits and vegetables (800 g/day) compared to lower consumption (200 g/day).[35] Fruits and vegetables, therefore, do not influence the risk of CRC. Fruits and vegetables provide a variety of nutrients and protective constituents such as carotenoids, Vitamin C, Vitamin E, folic acid, or fiber.[36]

Controls consumed significantly more green tea infusion than patients. Our results are consistent with several studies that demonstrate a reduction in CRC risk by consuming green tea rich in polyphenols.[37] However, other authors have found contradictory results. Indeed, in a Japanese study, Suzuki *et al*.[38] found no significant association between tea consumption and the occurrence of CRC. Another American study published in 2002 showed that the daily consumption of one to two cups of tea reduced the risk of colon cancer by 42%. Indeed, the polyphenolic compounds of green tea inhibit the development of cancer and its propagation.[38] The protective effects of tea are also due to its richness in flavonols, catechins, and theaflavins. These compounds can exert their protection against CRC by increasing colon motility and antioxidant status. Our study has some limits, perhaps most importantly, the retrospective nature of the study and the small sample. Establishing a cause-effect relationship may be difficult.

Conclusions

Through the results of our study, it was found that anorexia was almost constant in our patients and a state of risk of moderate or severe malnutrition almost 80% regardless of the score used. Patient energetic and protein intakes were less than recommended. Deficiencies in minerals, vitamins, and trace elements were also very common in our population. Therefore, early medical intervention accompanied by nutritional monitoring for patients is essential to avoid the installation of undernutrition. Our study identified frequently consumed foods by patients compared to controls: red meats, black tea, meats, offal, frying, and sweets. Furthermore, certain foods were more consumed by the controls: green tea, fruits, and cereals which are CRC protective food. Nutritional education programs on the role of food in CRC development and prevention through promoting a balanced, varied, and healthy diet and promoting daily physical activity are greatly needed. Similarly, early medical intervention accompanied by nutritional monitoring for patients is essential to avoid the installation of undernutrition.

Authors' contribution

All authors contributed to the conception, planning, conduct of the study, drafting and revising of the manuscript, and approval of its last version.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

This work has been approved by the Ethics Committee of the National Institute of Nutrition of Tunisia. Patients and controls provided informed consent for participation in the study.

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