Observational Study

Medicine®

OPEN

Association between dietary patterns and disease recurrence in Thai colorectal cancer patients

Vorraaud Kunnavuttivanich, MD[a], Pornpoj Pramyothin, MD[b], Suthinee Ithimakin, MD[a,*]

Abstract

Beside established anti-cancer treatment, dietary modification is one of the most promising approaches for reducing the probability of colorectal cancer (CRC) recurrence. Many Western studies showed a relationship between shortened survival and increased amounts of Western diet (meat and processed meat). Given that Thai food is dissimilar to Western diet, we aimed to explore the association between dietary patterns and disease recurrence among Thai CRC patients.

Early-stage CRC patients who were disease-free at the end of a 2-year period or patients with disease recurrence within 2 years were enrolled. Patients were administered a food frequency questionnaire to evaluate their dietary lifestyle. Quantitative comparison within individual food groups among patients who were disease-free and among those with recurrence was performed. Proportion of patients with recurrence and disease-free survival was compared between patients who had consumed the lowest and highest tertile of each dietary pattern.

A total of 225 CRC patients were enrolled (151 disease-free and 74 recurrence). There were no significant differences in demographic or tumor parameters between patients with or without disease recurrence. From the questionnaire, 45 food items were assigned to 1 of 12 food groups according to similarity in nutritional profile. Patients who consumed high amounts of pickled fish or chili-paste had significantly lower recurrence rates compared to patients who had never eaten those foods ($P < .01$). From the factor analysis, meat/wheat, vegetarian, and fast-food/processed fruit patterns were identified as the major dietary patterns. There was no significant association between intakes of individual dietary patterns and CRC recurrence.

Among CRC patients with Thai dietary lifestyles there was no association between meat/wheat, fast-food/processed fruit, or vegetarian dietary patterns and CRC recurrence. Greater consumption of some unique Thai foods, such as chili-paste or pickled fish, may relate to better outcomes for CRC patients.

Abbreviations: CI = confidence interval, CRC = colorectal cancer, DFS = disease-free survival, FFQ = food frequency questionnaire, HR = hazard ratio, LAB = lactic acid bacteria.

Keywords: colorectal cancer, dietary pattern, recurrence

1. Introduction

Colorectal cancer (CRC) is the third and fifth most common cancer in Thai men and women, respectively.[1] Surgical treatment and adjuvant chemotherapy in colon cancer patients, with the addition of radiotherapy in rectal cancer patients, reduce disease recurrence and prolong survival. Surveillance via serum tumor markers, annual abdominal imaging, and periodic colonoscopy are recommended to detect early recurrence, at which point curative resection is possible.

One of the most pressing concerns after completion of adjuvant therapy is how patient lifestyle modifications, especially dietary change, might reduce colon cancer recurrence. Several studies and systematic reviews have demonstrated that a Western diet is associated with higher incidence of colon cancer development, whereas diets rich in fiber and lower in red meat have protective effects against colon cancer occurrence.[2–6]

There are few studies from Western countries regarding the effects of dietary patterns on CRC disease recurrence. Zhu et al explored the relationship of processed meat, prudent, and high-sugar dietary patterns to CRC recurrence. A processed meat dietary pattern, which was defined as high intake of processed red meat and fish, was associated with higher risk of recurrence and death in CRC patients.[7] In contrast, there was no association between prudent or high-sugar patterns and oncological outcomes. In another study, prospective dietary pattern analyses were performed using semi-quantitative FFQs at 6 months after completion of adjuvant treatment in patients recruited from the CALGB 8980 study.[8] In this cohort, dietary patterns were explored in terms of Western and prudent patterns. The authors reported significantly higher CRC recurrence and death among patients who consumed the highest quintile of Western diet compared to the lowest quintile with a hazard ratio (HR) of 2.85 and 2.32, respectively. Again, no association between the prudent

Editor: Eric Bush.

Funding source: Routine to Research grant, Faculty of Medicine Siriraj Hospital.

The authors have no conflicts of interest to disclose.

[a] Division of Medical Oncology, [b] Division of Nutrition, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

[*] Correspondence: Suthinee Ithimakin, Chalermprakiat Building, 13th floor, Siriraj Hospital, 2 Wanglang Rd, Bangkoknoi, Bangkok 10700, Thailand (e-mail: Aesi105@yahoo.co.th).

How to cite this article: Kunnavuttivanich V, Pramyothin P, Ithimakin S. Association between dietary patterns and disease recurrence in Thai colorectal cancer patients. Medicine 2020;99:11(e19522).

Received: 23 August 2019 / Received in final form: 3 December 2019 / Accepted: 9 February 2020

http://dx.doi.org/10.1097/MD.0000000000019522

dietary pattern and disease recurrence was found.[8] Another cohort from the United States showed higher all-cause mortality among non-metastatic CRC patients who consumed greater amounts of red and processed meats prior to diagnosis, but no association with diet patterns was observed during the pre-diagnostic and post-diagnostic periods.[9] Several observational studies suggest that adequate physical activity is another possible method to lower the risk of CRC recurrence.[10–13] To date, there is no randomized controlled study to confirm the benefit of exercise in terms of cancer recurrence and prolonged survival. However, it is consistent among trials that exercise is safe and feasible for both early-stage and metastatic CRC patients.[14]

Due to relatively positive dietary practices among the Asian population in terms of greater consumption of vegetables and fruits and less fat intake,[15] recommendations of dietary modifications based on Western studies may not be relevant to Thai cancer patients. To the best of our knowledge, there is currently no study exploring the association between dietary patterns and disease recurrence among Thai cancer patients. This study aims to explore whether dietary patterns associate with CRC recurrence in Thai CRC patients, with a primary objective of comparing proportions of CRC recurrence among patients who have consumed different amounts of each diet pattern. The secondary objective was to compare the intake of different food groups between disease-free and recurrence patients. The results of this study may be valuable for guiding non-pharmacological management in non-metastatic Thai CRC patients.

2. Materials and methods

2.1. Study design and participants

This retrospective case control study included patients with stage II-III CRC who completed multimodality curative treatment and received or currently receive regular follow-up examinations at Siriraj Hospital. The patients were asked to enroll in the study once they were disease-free after 2 years or once they had experienced disease recurrence within that timeframe. Patients who remained disease-free after 2 years were considered the control group to be compared with patients who experienced disease recurrence within 2 years after completion of adjuvant therapy. The patients with incomplete clinical data were ineligible. The study protocol was approved by the Institutional Review Board of Siriraj Hospital (approval No. 432/2559). Written informed consent was acquired from each participant.

2.2. Methods

The food frequency questionnaire (FFQ), a validated assessment tool adapted for Thai patients,[16] was administered upon enrollment to examine each patient's regular dietary behavior and routine physical activities. Patients received assistance from an oncology fellow or a research interviewer to aid in their understanding of the questionnaire as necessary. The FFQ included queries regarding 45 Thai food items that were validated by the 4th National Health Examination Survey, along with food indigenous to the Thai population, such as pickled fish/meat and processed fruits. The questionnaire was designed to assess the patients' frequency and semi-quantitative intake of each food item. In addition to the FFQ, the globally published questionnaire of physical activities GPAQ Version 2[17] was used for data collection.

Baseline characteristics including age, gender, tumor stage, and previous treatment were collected at enrollment. The FFQ consisted of 2 sections, each addressing the frequency and quantity of individual food items consumed by the patients. For each food item, the patients were asked to estimate their frequency and intake between the time of CRC diagnosis and enrollment in the study. Food frequency was divided into the following 7 categories: never, less than once per month, 1 to 3 times per month, 1 to 3 times per week, 4 to 6 times per week, once a day, and more than once per day. The patients' approximate food quantity intake was assessed by inquiries using universal measurement units, for example, tablespoon(s) for meat and scoop(s) for rice. The portion sizes of specific foods were depicted in photographs and, in some cases, patients were shown real containers as a reference. To calculate consumption and energy intake for each food item, the frequency of consumption was multiplied by the nutrient content of 1 portion size according to nutritional values from the Thai food table.[18] For the physical activity assessment, a questionnaire adopted from GPAQ V2 was used according to the original user manual.[17] Higher than 600 metabolic equivalent min per week was defined as adequate physical activity.[11]

2.3. Statistical analysis

Baseline characteristics including age, gender, stage, previous treatment, family history of CRC, and physical activity are descriptively presented as results from Chi-Squared analyses. The total caloric intake of each food group was calculated by multiplying the frequency and quantity of single intake adjusted into "per month" units. Associations between intake of various food groups and CRC recurrence were assessed by the Mann–Whitney *U* test. Chi-Squared test was used to compare proportion of patients with disease recurrence in each tertile of individual food group intake.

We classified 45 food items from the FFQ into 12 food groups based on similarity of macronutrient components (Table 1). Exploratory principal factor analyses were used to identify major dietary patterns based on the 12 predefined food groups. A varimax rotation was used to produce uncorrelated and easily interpretable components to illustrate the greatest proportion of the 12 predefined food groups. Dietary patterns were identified

Table 1

Classified food groups.

Food groups	Example items
Red meat	Red meat with fat, red meat without fat, entrails, meat products, e.g., sausage, shredded dried pork, etc.
White meat	Poultry with or without skin, fish and its byproducts, seafood
Soy and bean	Nuts/grains, soy milk
Eggs	Eggs
Wheat	White rice, brown rice, sticky rice, noodles, instant noodles, white bread, whole-wheat bread
Fast-food	Fried food, fast-food
Processed fruit	Welding fruit, preserved fruit, compote fruit
Dairy products	Natural yogurt, flavored yogurt, yogurt drinks, fresh milk, flavored milk, low-fat milk
Sweet drinks	Sweetened drinks, seasoned coffee, fruit/vegetable juice
Sweets	Sweets, Thai sweets, syrup, honey, coconut milk sweets, snacks
Thai condiments	Pickled fish, chili-dip/paste
Fruits/veggies	Fresh fruits, vegetables

according to food groups that rotated by a factor greater than or equal to 0.5 and exhibited an eigenvalue greater than 1.2. Each dietary pattern was composed of all food groups with different factor loadings, that is, ., the relative weight of each food group's contribution to each food pattern. Major food groups in each food pattern were defined as groups with loading factors greater than or equal to 0.5.

To calculate the intake within each food pattern, we used a summation of the products derived from multiplying between the loading factor and frequency of intake. We divided the quantity of each food component into tertiles, which implied the quantitative range of the component. Then, the proportions of patients with disease recurrence within the highest and the lowest tertile of each food component were compared by Chi-Squared tests. Furthermore, odds ratios (OR) and 95% confidence intervals (CI) for disease recurrence were reported for patients consuming various amounts of the food components using the lowest tertile as a reference. Analyses were performed using SPSS version 18.

According to the results of a previous study,[8] the adjusted HR for CRC recurrence or death among patients consuming the highest quintile of Western diet compared with the lowest quintile was 2.58 with a 95% CI of 1.75 to 4.63. The necessary sample size for the present study was calculated using the aforementioned data as guidance. As a result, 67 participants were required for each tertile to achieve 80% power in detecting an OR of 3 for CRC recurrence when comparing between patients who consumed high amounts of particular dietary patterns and the reference group. A *P*-value less than .05 was considered statistically significant based on a 2-tail analysis. Multivariate analyses were performed to identify factors related to recurrence while adjusting for known prognostic and confounding factors such as stage, previous treatment, and physical activity. Disease-free survival (DFS) rates in subgroups of patients consuming different amounts of particular dietary patterns were analyzed using log rank tests and the Kaplan-Meier method.

3. Results

There were 225 stage II and III CRC patients enrolled in the study who completed adjuvant therapy and received follow-up examinations at Siriraj Hospital from January 2015 to January 2018. All participants provided written and informed consent when recruited for the study. At the time of enrollment, 151 patients (67%) were disease-free while 74 (33%) experienced disease recurrence. There was no significant difference in baseline characteristics, previous treatment, or physical activity between 2 groups (Table 2).

We explored the intake of each food group between patients with and without disease recurrence. Disease-free patients consumed similar amounts of protein, wheat, sweet items, fruits, and vegetables compared with patients who experienced disease recurrence (Table 3). Furthermore, patients who consumed more indigenous Thai items, such as chili-paste or pickled fish, experienced a lower chance of disease recurrence. A total of 129 patients (57.3%) reported previous consumption of Thai condiments with a median intake of 200 Kcal/mo. Since there was extreme deviation in Thai condiments intake, Thai condiments consumption was categorized into the following 3 groups: no intake, <400 Kcal/mo, and ≥400 Kcal/mo. The multivariate analysis showed an association between CRC recurrence and greater than 400 Kcal/mo intake of Thai condiments with an OR of 0.39 ($P < .01$, 95% CI 0.2–0.79) adjusted for colon cancer parameters and physical activity.

To identify major dietary patterns, 12 predefined food groups were evaluated by factor analyses. As a result, we obtained 3 main dietary patterns, meat/wheat, fast-food/processed food, and

Table 2

Baseline patient characteristics.

Patient characteristics	Disease recurrence status		*P*-value
	No (N = 151)	Yes (N = 74)	
Gender, n (%)			
Male	82 (54.3)	34 (45.9)	.15
Female	69 (45.7)	40 (54.1)	
Age, n (%)			
<65 yr	70 (46.4)	42 (56.8)	.09
≥65 yr	81 (53.6)	32 (43.2)	
Stage, n (%)			
2	62 (41.1)	24 (32.4)	.13
3	89 (58.9)	50 (67.6)	
Primary site, n (%)			
Colon	84 (55.6)	38 (51.3)	.32
Rectum	67 (44.4)	36 (48.6)	
Adjuvant chemotherapy, n (%)			
Oxaliplatin/fluoropyrimidine	59 (39.1)	32 (43.2)	.32
Fluoropyrimidine	92 (60.9)	42 (56.8)	
Adjuvant radiotherapy, n (%)			
No	83 (55)	46 (62.2)	.51
Yes	45 (45)	26 (37.8)	
Physical activity, n (%)			
<600 MET/wk	25 (16.6)	15 (20.3)	.31
>600 MET/wk	126 (83.4)	59 (79.7)	

MET = metabolic equivalent.

Table 3

Intake of individual food groups.

Food groups	Recurrence at 2 yr	Number of patients with disease recurrence			P-value
		1st tertile	2nd tertile	3rd tertile	
Red meat	Yes	29	18	27	.13
	No	46	57	48	
White meat	Yes	26	22	26	.73
	No	49	53	49	
Soy bean	Yes	27	26	21	.49
	No	49	47	55	
Eggs	Yes	41	25	8	.55
	No	89	52	10	
Wheat	Yes	23	24	27	.69
	No	55	48	48	
Fast-food	Yes	52		22	.48
	No	99		52	
Processed fruit	Yes	45		29	.16
	No	106		45	
Dairy	Yes	47		27	.48
	No	103		48	
Sweet drink	Yes	22	29	23	.55
	No	51	48	52	
Sweet pieces	Yes	21	24	29	.54
	No	54	43	54	
Thai condiments	Yes	69	5	0.008	
	No	120	31		
Fruits/vegetables	Yes	26	23	25	.87
	No	49	52	50	

Table 4

Assessment of factor loading in factor analyses of dietary intake and colon cancer recurrence.

Food groups	Factors*		
	Meat and wheat pattern	Vegetarian pattern	Fast/processed foods
Red meat	0.72	−0.01	0.18
White meat	0.47	0.39	0.07
Wheat	0.59	−0.12	0.23
Egg	0.62	0.14	−0.23
Thai condiments	0.26	0.37	0.48
Processed fruit	0.08	−0.02	0.52
Fast-food	0.18	−0.32	0.62
Sweet drinks	0.14	−0.06	−0.14
Soy beans	−0.14	0.55	0.01
Fruits/vegetables	0.20	0.70	−0.06
Sweets	0.36	−0.37	−0.10
Dairy	0.27	−0.18	−0.56

* Values ≥0.5 are indicated as the main components of food groups.

vegetarian, with an eigenvalue greater than 1.2 that accounted for 38% of all possible food components (Table 4). The meat/wheat dietary pattern primarily consisted of red meat and wheat, while the vegetarian dietary pattern mainly consisted of fruits, vegetables, and soybeans. The fast-food/processed fruit pattern was identified as another main dietary component.

There was no statistical difference in intake of the meat/wheat dietary pattern among patients with different genders, ages, and cancer stages (Table 5). Furthermore, there was no difference in disease recurrence or DFS between patients who consumed the highest and lowest tertile of the meat/wheat pattern (Fig. 1a).

There was a significantly higher proportion of patients with relatively high physical activity consuming greater amounts of the vegetarian dietary pattern. There was a higher proportion of patients with earlier stage CRC consuming greater amounts of vegetarian patterns. Again, there was no difference in disease recurrence among patients who consumed different amounts of the vegetarian dietary pattern (Table 6). The multivariate analysis revealed no association between intake of the vegetarian pattern

Table 5

Association between baseline characteristics, CRC recurrence, and the meat/wheat dietary pattern.

		Meat/wheat pattern			
		1st tertile (n = 74)	2nd tertile (n = 75)	3rd tertile (n = 76)	*P*-value
Disease status	No recurrence	53	49	49	.58
	Recurrence	21	26	27	
	OR (95% CI)	1 (reference)	1.4 (0.69, 2.87)	1.401 (0.68, 2.9)	
Age	≤65 yr	29	38	45	.21
	>65 yr	45	37	31	
	OR (95% CI)	1 (reference)	0.73 (0.36, 1.48)	0.517 (0.25, 1.07)	
Gender	Male	33	38	45	.13
	Female	41	37	31	
	OR (95% CI)	1 (reference)	0.75 (0.389, 1.44)	0.5 (0.25, 0.98)	
Stage	2	26	33	27	.25
	3	48	42	49	
	OR (95% CI)	1 (reference)	0.524 (0.24, 1.17)	0.597 (0.26, 1.38)	
Chemotherapy regimen	Oxaliplatin-based	24	29	38	.13
	Fluoropyrimidine	50	46	39	
	OR (95% CI)	1 (reference)	0.55 (0.23,1.32)	0.41 (0.17,0.98)	
Physical activity	<600 MET/wk	11	11	18	.16
	≥600 MET/wk	63	64	58	
	OR (95% CI)	1 (reference)	0.93 (0.37, 2.35)	0.47 (0.2, 1.13)	

CI = confidence interval, CRC = colorectal cancer, MET = metabolic equivalent, OR = odds ratios.

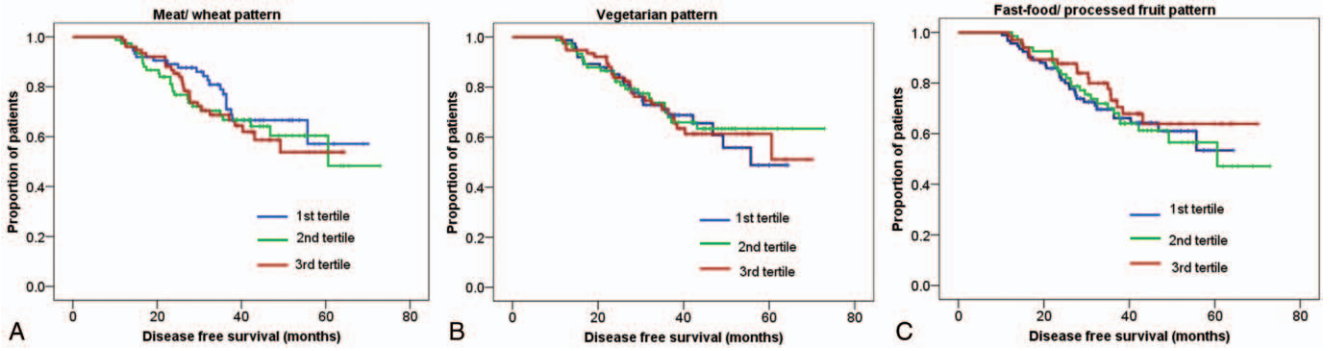

Figure 1. Disease-free survival of subgroups with different amounts of meat/carbohydrate (1a), vegetarian (1b), and fast-food/processed fruit (1c) dietary pattern consumption. Each curve represents different amounts of intake ranging from 1st to 3rd tertile as the lowest to highest amount of intake.

Table 6

Association between baseline characteristics, CRC recurrences, and the vegetarian pattern.

		Vegetarian pattern			
		1st tertile (n = 74)	2nd tertile (n = 75)	3rd tertile (n = 76)	*P*-value
Disease status	No recurrence	49	52	50	.85
	Recurrence	25	23	26	
	OR (95% CI)	1 (reference)	0.93 (0.46, 1.89)	1.14 (0.56, 2.35)	
Age	≤65 yr	36	32	44	.4
	>65 yr	38	43	32	
	OR (95% CI)	1 (reference)	1.57 (0.77, 3.2)	1.07 (0.51, 2.22)	
Gender	Male	37	41	38	.8
	Female	37	34	38	
	OR (95% CI)	1 (reference)	0.84 (0.43, 1.61)	1.03 (0.53, 2.02)	
Stage	2	26	25	35	.04
	3	48	50	41	
	OR (95% CI)	1 (reference)	0.82 (0.36, 1.84)	0.33 (0.14, 0.81)	
Chemotherapy regimen	Oxaliplatin-based	25	31	35	.02
	Fluoropyrimidine	49	44	41	
	OR (95% CI)	1 (reference)	0.64 (0.27,1.54)	0.26 (0.1,0.68)	
Physical activity	<600 MET/wk	20	15	5	<.01
	≥600 MET/wk	54	60	71	
	OR (95% CI)	1 (reference)	1.6 (0.73, 3.49)	5.64 (1.92, 16.48)	

CI = confidence interval, CRC = colorectal cancer, MET = metabolic equivalent, OR = odds ratios.

and CRC recurrence. There was no statistical difference in DFS between patients with high or low intake of the vegetarian dietary pattern (Fig. 1b).

Furthermore, the factor analysis revealed no association between the fast-food/processed fruit pattern and disease recurrence, and there was no difference in DFS among patients consuming different amounts of this dietary pattern (Table 7, Fig. 1c).

4. Discussion

Three distinct dietary patterns, meat/wheat, vegetarian, and fast-food/processed fruit, were generated in this case control study. We demonstrated that varying amounts of each dietary pattern did not affect disease recurrence among operable CRC patients. Interestingly, when analyses were performed within the individual food groups, patients who consumed high amounts of distinctly Thai foods, e.g., chili-paste or pickled fish, exhibited lower incidences of disease recurrence. Increasing consumption of meats, sweets, wheat, fruits, or vegetables was not a potentiating or protective factor for disease recurrence. However, a multivariate analysis to adjust for other known prognostic factors in CRC recurrence showed no significant difference in cancer recurrence among patients with various intakes of each food group.

Although the association between the Western diet, which is abundant in meat and high in carbohydrates, and a greater chance of CRC occurrence has been consistently reported,[2,5,6] information regarding the relationship of dietary patterns and

Table 7

Association between baseline characteristics, CRC recurrence, and processed food pattern.

		Fast-food/ processed fruit pattern			
		No intake (n = 74)	Low intake (n = 75)	High intake (n = 76)	*P*-value
Disease status	No recurrence	61	42	48	.34
	Recurrence	31	25	18	
	OR (95% CI)	1 (reference)	1.22 (0.54, 2.15)	0.46 (0.3, 1.32)	
Age	≤65 yr	36	36	40	.07
	>65 yr	56	31	26	
	OR (95% CI)	1 (reference)	0.64 (0.32, 1.3)	0.43 (0.2, 0.9)	
Gender	Male	55	25	36	.02
	Female	37	42	30	
	OR (95% CI)	1 (reference)	2.54 (1.31, 4.92)	1.23 (0.63, 2.42)	
Stage	2	31	29	26	.09
	3	61	38	40	
	OR (95% CI)	1 (reference)	0.49 (0.21, 1.09)	0.43 (0.18, 1.02)	
Chemotherapy regimen	Oxaliplatin-based	31	27	33	.23
	Fluoropyrimidine	61	40	33	
	OR (95% CI)	1 (reference)	0.65 (0.27,1.55)	0.48 (0.19, 1.17)	
Physical activity	<600 MET/wk	13	8	19	<.01
	≥600 MET/wk	79	59	470	
	OR (95% CI)	1 (reference)	1.1 (0.41, 2.94)	0.32 (0.14, 0.74)	

CI = confidence interval, CRC = colorectal cancer, OR = odds ratios.

CRC recurrence are limited and controversial. The association between dietary patterns and CRC recurrence and mortality was assessed using a factor analysis to define 2 distinct food patterns, the Western dietary pattern, and the prudent dietary pattern. The authors concluded that the Western pattern may be related to a higher risk of recurrence and death among patients with stage III colon cancer.[8] In addition, some studies suggest that higher consumption of red and processed meats is related to higher mortality in early CRC patients.[7,9] On the other hand, another study from France showed that higher energy intake is associated with longer survival among CRC patients with unclear mechanisms.[19]

Several previous studies about diet and CRC recurrence were based on pre-diagnostic diet intake, which may not represent a true lifestyle modification for prevention of cancer recurrence.[7,19] Although no interaction between pre-diagnostic and post-diagnostic consumption was demonstrated in a previous study,[9] it is still unclear whether this result is applicable to other studies. From our perspective, dietary patterns obtained from patients in the post-diagnostic period would be more accurate and applicable to identify their association to cancer recurrence.

Another major concern in providing lifestyle modification recommendations based on the results of previous studies in patients with CRC is that the conclusions were drawn from data of Western countries, which predominantly adhere to different dietary patterns than that of Thai or Asian countries. Assuming that Thai or Asian populations consume less meat and carbohydrates relative to Western populations, Thai patients who consume the highest quintile of meat or carbohydrates may be ranged in the low or middle quintile if classified by the same criteria of Western countries. To the best of our knowledge, there is no previous study comparing the food components of Asian and Western diets. Therefore, we conducted the first study analyzing dietary patterns among Thai CRC patients to assess the association between dietary patterns and disease recurrence.

In the present study, consumption of condiments that are unique to Thailand and Southeast Asia was associated with lower incidence of CRC recurrence. These condiments included chili paste and pickled fish in brine and rice called *Pla-ra* and *Pla-jao*[20] which are native to the central, north, and northeastern parts of Thailand. Such condiments differ from other fermented fish products in that addition of rice carbohydrate allows for lactic acid fermentation which contributes to prolonged shelf-life.[21] Microbiological analysis performed on commercially available *Pla-ra* and *Pla-jao* products showed enrichment of lactic-acid bacteria (LAB) of 7.32 and 7.76 counts/g $^{(\log 10)}$, respectively.[20] Recent studies have demonstrated the abilities of LAB to regulate apoptosis and inflammatory pathways of colon adenocarcinoma cells.[22,23] It has also been proposed that the protective properties of LAB against colon cancer may be mediated through reduced DNA damage as a result of antioxidation, epigenetics, and an increase in local production of short-chain fatty acids, particularly propionic and butyric acids.[24]*Pla-ra* and *Pla-jao* are occasionally consumed raw and may provide a dietary source of live organisms.[25] It is intriguing to postulate that the association observed was mediated by alterations in the intestinal microbiota promoted by consumption of *Pla-ra* and *Pla-jao*; however, more rigorous studies are required to test this hypothesis. In addition to pickled fish, chili-paste may also have protective effects against colorectal cancer, as previous studies have demonstrated that capsaicin, a primary ingredient of chili, induced apoptosis in a human cancer cell line.[26] Other mechanisms proposed to mediate anticancer effects of capsaicin include regulation of cell cycle, angiogenesis, and inhibition of matrix metalloproteinases and epithelial mesenchymal transition enzymes which mitigate tumor metastasis.[27] However, a recent case-control study did not demonstrate relationship between chili pepper consumption and colorectal cancer risk.[28] Further studies are required to assess effects of chili consumption on disease recurrence in colorectal cancer patients.

There were some limitations to our study. Firstly, the study was conducted with a limited sample size, leading to a restriction of power to demonstrate the differences in CRC recurrence among dietary patterns. Secondly, we used a questionnaire that required the patient to recall dietary patterns for up to 2 years prior, which was possibly confounded by recall bias. In addition, we have not performed a 24-hour dietary recall to validate the questionnaire. Also, we have not explored dietary pattern before diagnosis of CRC which may be change into the healthier way. However, we did exclude patients who reported a change in dietary lifestyle between the time of diagnosis to the period of enrollment. Lastly, dietary intake as a quantitative value was obtained from calculations of intake frequency multiplied by estimates of amounts of each meal using a caloric table instead of a 24-hour dietary recall, which may be a more accurate measure.

Despite these few limitations, the results of our study may be crucial for Thai CRC patients as a guidance for dietary intake aiming to prevent or delay recurrence after CRC diagnosis. We will apply these data to clinical practice via recommendations to non-metastatic CRC patients, providing an evidence-based answer to the common questions regarding dietary modification after diagnosis of CRC. We will ensure that patients consume typical Thai foods without any type of diet restriction or preference as a tool to reduce cancer recurrence. Furthermore, our findings may adjust false beliefs about specific food restrictions that contribute to malnutrition and worsen quality of life.

5. Conclusions

There was no significant association between the meat/wheat, vegetarian or fast-food/processed fruit dietary patterns, and disease recurrence. Notably, patients who consumed high amounts of distinctly Thai foods, e.g., chili-paste or pickled fish, exhibited significantly lower incidences of disease recurrence. Therefore, the consumption of Thai food without specific restrictions or preferences is recommended for non-metastatic CRC patients.

Acknowledgments

We thank Professor Dr Wichai Aekplakorn of the Department of Community Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, and Assistant Professor Dr Warapone Satheannoppakao of the Department of Nutrition, Faculty of Public Health, Mahidol University, for allowing the use of FFQs which they developed and for kindly providing very helpful suggestions. We thank Ms Nanta Khumkhana and Ms Wanjan Deekum for their assistance with preparation of questionnaires and case record forms. We thank Mr Suthipol Udompunthurak for consultations regarding statistical analysis and Miss Ananya Srisomnnuek for facilitating patient recruitment and data collection. We thank Dr Jirawat Thanestada for kind help regarding technical graphic issue.

Author contributions

Conceptualization: Pornpoj Pramyothin, Suthinee Ithimakin.
Data curation: Vorraaud Kunnavuttivanich, Suthinee Ithimakin.
Formal analysis: Vorraaud Kunnavuttivanich, Suthinee Ithimakin.
Funding acquisition: Suthinee Ithimakin.
Methodology: Vorraaud Kunnavuttivanich, Pornpoj Pramyothin, Suthinee Ithimakin.
Project administration: Suthinee Ithimakin.
Resources: Suthinee Ithimakin.
Supervision: Pornpoj Pramyothin, Suthinee Ithimakin.
Validation: Suthinee Ithimakin.
Writing–original draft: Vorraaud Kunnavuttivanich, Suthinee Ithimakin.
Writing–review & editing: Vorraaud Kunnavuttivanich, Pornpoj Pramyothin, Suthinee Ithimakin.
Suthinee Ithimakin orcid: 0000-0002-4205-6112.

References

[1] Khuhaprema T, Srivatanakul P. Colon and rectum cancer in Thailand: an overview. Jpn J Clin Oncol 2008;38:237–43.
[2] Slattery ML, Boucher KM, Caan BJ, et al. Eating patterns and risk of colon cancer. Am J Epidemiol 1998;148:4–16.
[3] Godos J, Bella F, Torrisi A, et al. Dietary patterns and risk of colorectal adenoma: a systematic review and meta-analysis of observational studies. J Hum Nutr Diet 2016;29:757–67.
[4] Huxley RR, Ansary-Moghaddam A, Clifton P, et al. The impact of dietary and lifestyle risk factors on risk of colorectal cancer: a quantitative overview of the epidemiological evidence. Int J Cancer 2009;125:171–80.
[5] Magalhaes B, Peleteiro B, Lunet N. Dietary patterns and colorectal cancer: systematic review and meta-analysis. Eur J Cancer Prev 2012;21:15–23.
[6] Vulcan A, Brandstedt J, Manjer J, et al. Fibre intake and incident colorectal cancer depending on fibre source, sex, tumour location and tumour, node, metastasis stage. Br J Nutr 2015;114:959–69.
[7] Zhu Y, Wu H, Wang PP, et al. Dietary patterns and colorectal cancer recurrence and survival: a cohort study. BMJ Open 2013;3: e002270.
[8] Meyerhardt JA, Niedzwiecki D, Hollis D, et al. Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. JAMA 2007;298:754–64.
[9] McCullough ML, Gapstur SM, Shah R, et al. Association between red and processed meat intake and mortality among colorectal cancer survivors. J Clin Oncol 2013;31:2773–82.
[10] Backman M, Wengstrom Y, Johansson B, et al. A randomized pilot study with daily walking during adjuvant chemotherapy for patients with breast and colorectal cancer. Acta Oncol 2014;53:510–20.
[11] Courneya KS, Booth CM, Gill S, et al. The Colon Health and Life-Long Exercise Change trial: a randomized trial of the National Cancer Institute of Canada Clinical Trials Group. Curr Oncol 2008;15:279–85.
[12] Courneya KS, Friedenreich CM, Quinney HA, et al. A randomized trial of exercise and quality of life in colorectal cancer survivors. Eur J Cancer Care 2003;12:347–57.
[13] Pinto BM, Papandonatos GD, Goldstein MG, et al. Home-based physical activity intervention for colorectal cancer survivors. Psychooncology 2013;22:54–64.
[14] van Blarigan EL, Meyerhardt JA. Role of physical activity and diet after colorectal cancer diagnosis. J Clin Oncol 2015;33:1825–34.
[15] Lesser IA, Gasevic D, Lear SA. The association between acculturation and dietary patterns of South Asian immigrants. PloS One 2014;9: e88495.
[16] Aekplakorn W, Satheannoppakao W, Putwatana P, et al. Dietary pattern and metabolic syndrome in Thai adults. J Nutr Metab 2015;2015: 468759.
[17] Cleland CL, Hunter RF, Kee F, et al. Validity of the global physical activity questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. BMC Public Health 2014;14:1255.
[18] Nutrition Division DoHMoPH. Nutritive Values of Thai Foods 2001; http://nutrition.anamai.moph.go.th/images/files/nutritive_values_of_thai_foods.pdf.
[19] Dray X, Boutron-Ruault MC, Bertrais S, et al. Influence of dietary factors on colorectal cancer survival. Gut 2003;52:868–73.
[20] Adams MR, Cooke RD, Rattagool P. Fermented fish products of Southeast Asia. Bangkok, Thailand: Department of Fisheries, Ministry of Agriculture and Cooperatives; 1991.
[21] El-Ghaish S, Ahmadova A, Hadji-Sfaxi I, et al. Potential use of lactic acid bacteria for reduction of allergenicity and for longer conservation of fermented foods. Trends Food Sci Tech 2011;22:509–16.
[22] Bohlul E, Hasanlou F, Taromchi AH, et al. TRAIL-expressing recombinant lactococcus lactis induces apoptosis in human colon adenocarcinoma SW480 and HCT116 cells. J Appl Microbiol 2019; 126:1558–67.
[23] El-Deeb NM, Yassin AM, Al-Madboly LA, et al. A novel purified Lactobacillus acidophilus 20079 exopolysaccharide, LA-EPS-20079, molecularly regulates both apoptotic and NF-κB inflammatory pathways in human colon cancer. Microb Cell Fact 2018;17:29.
[24] Zhong L, Zhang X, Covasa M. Emerging roles of lactic acid bacteria in protection against colorectal cancer. World J Gastroenterol 2014;20: 7878–86.
[25] Rezac S, Kok CR, Heermann M, et al. Fermented foods as a dietary source of live organisms. Front Microbiol 2018;9:1785.
[26] Kim CS, Park WH, Park JY, et al. Capsaicin, a spicy component of hot pepper, induces apoptosis by activation of the peroxisome proliferator-activated receptor gamma in HT-29 human colon cancer cells. J Med Food 2004;7:267–73.
[27] Clark R, Lee SH. Anticancer properties of capsaicin against human cancer. Anticancer Res 2016;36:837–43.
[28] Yang Y, Zhang J, Weiss NS, et al. The consumption of chili peppers and the risk of colorectal cancer: a matched case-control study. World J Surg Oncol 2019;17:71.