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PRO-INFLAMMATORY DIET AND RISK OF COLORECTAL AND BLADDER CANCER: EPIDEMIOLOGICAL EVIDENCE

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ABSTRACT

Introduction:
Colorectal cancer (CRC) is the third most prevalent cancer worldwide, and urinary bladder cancer (BC) ranks as the tenth most common. Chronic inflammation has been recognized as a significant contributor to cancer development. Diets rich in red and processed meats, sugars, refined grains, and saturated fats—collectively referred to as pro-inflammatory diets—are known to promote systemic inflammation, which may influence cancer risk.

Methodology:
This review aims to explore the association between pro-inflammatory diets and the risk of CRC and BC using dietary inflammatory scores: the Dietary Inflammatory Index (DII) and the Empirical Dietary Inflammatory Index (EDII). A systematic search was conducted in PubMed up to October 2022. Human epidemiological studies that employed DII or EDII scores and reported effect estimates (OR, HR, or RR with 95% CI) for CRC or BC were included. A total of 19 studies met the inclusion criteria.

Results:
Ten case-control and four cohort studies assessed the link between pro-inflammatory diets and CRC, all reporting a positive association. For BC, two case-control studies demonstrated a positive link, while three cohort studies did not find a statistically significant relationship.

Conclusion:
There is consistent evidence supporting a strong positive association between pro-inflammatory diets and increased CRC risk. However, findings related to BC are inconclusive, with conflicting results between study types. Further large-scale prospective studies and pragmatic clinical trials are needed, particularly to better understand the dietary impact on BC risk and to confirm causality in CRC.

INTRODUCTION

Colorectal cancer is the second most fatal and third most prevalent cancer diagnosis for both genders together [1]. Colorectal cancer is a type of cancer that gastrointestinal cancer and can affect either the colon or the rectum [2]. With 1.85 million new cases/year (10.2% of total malignancies) worldwide, colorectal cancer is only preceded by lung (2.09 million new cases/year; 11.6% of total malignancies) and breast (2.08 million new cases/year; 11.6% of total malignancies) cancers according to International Agency for Research on Cancer (IARC) [2].

A series of risk factors are associated with CRC, including a family history of CRC or its related hereditary disease (e.g., Lynch syndrome, familial adenomatous polyposis), personal disease history (e.g., inflammatory bowel disease and diabetes), lifestyle and dietary habits (e.g., tobacco smoking, alcohol drinking, consumption of red and processed meat), and bacterial infection (e.g., Bacteroides fragilis, Escherichia coli). [3]. Among lifestyle factors, high levels of sedentary time are linked to an elevated risk of colorectal cancer, according to a 2018 Physical Activity Guidelines for Americans (PAGA) Committee analysis, which found only weak evidence of a dose-response relationship [4]. Regular consumers of alcohol have a nearly two-fold increased risk. Additionally, there was a positive correlation between BMI and colorectal cancer and a negative correlation between high levels of physical exercise and CRC. [5]. The risk of colon cancer is also higher among heavy cigarette smokers and those who consume red meat more than twice a day [6]. Nearly all of the information used to determine these risk factors comes from observational research.

Urinary bladder cancer BC is the tenth most common cancer diagnosis and the most frequent cancer in the urinary tract. 549,393 persons had BC diagnoses in 2018, and 199,922 died from the illness globally [7]. Incidence rates in both sexes are highest in Southern Europe (Greece, with the highest incidence rate in men globally; Spain; Italy), Western Europe (Belgium and the Netherlands), and North America, although the highest rates are estimated in Lebanon among women. Other than certain occupational exposures to chemical and water contaminants, cigarette smoking is the main risk factor for bladder cancer and, with the rising prevalence of smoking among women, the attributable risk, at least in the United States, has reached that among men, with 50% of bladder cancer cases attributable to smoking in both sexes [7]. Both the number of cigarettes smoked and the number of years a person smokes raise the risk. However, according to some reviews, former cigarette smokers seem to have a reduced incidence of urinary tract cancer as compared with current smokers [8]. Working with some aromatic amines such as α-naphthylamine, β-naththylamine, and benzidine has been linked to a greater incidence of bladder cancer. According to estimates based on these and other occupational risks, 5–10% of bladder cancer cases in industrialized nations were attributable to exposures related to the workplace [9].

In addition, in regions of the world where Schistosoma haematobium infestation is widespread, infectious agents have a significant impact on the risks of bladder cancer [10]. However, this only applies to squamous cell bladder cancer; urothelial bladder cancer is exempt. Consumption of processed meat, particularly bacon, sausage, and ham, was significantly linked to an elevated risk of bladder cancer, and dietary intake of grilled, salted, and tinned meat was also significantly linked to increased risks of bladder cancer whereas frequent daily urination, consumption of fruit juices and cabbage (h vs I fertile) were indicated as protective factors, however; not based on the World Cancer Research Fund (WCRF) report [11-12-55]. Furthermore, according to the dose-response study, increasing vegetable and fruit consumption by 200 g/day each reduced the incidence of BC by 8% and9%, respectively. Plus, high

consumption of black and green tea was not associated with increased risk of BC [54].

According to clinical and epidemiological data, inflammatory reactions are crucial for the onset and development of many chronic conditions, including cancer [13]. While it is known that inflammation plays a significant role in the development of CRC tumors, both in hereditary and sporadic tumors, there is growing evidence that treatment with anti-inflammatory drugs may avoid or postpone its onset [14]. Similarly, BC is a highly immunogenic malignancy, and cytokine-induced imbalances in the distribution and differentiation of tumor-infiltrating cytotoxic cells can boost bladder cancer cell proliferation [15]. Since inflammation may be linked to the development of both cancer types, it is of interest to investigate whether a less pro-inflammatory diet may decrease CRC and BC risk and vice versa.

It has been frequently found that diet can modulate inflammation. According to a growing body of research, a diet high in calories but low in nutrients may be linked to chronic, systemic inflammation and poor health [16]. It has been documented that eating a lot of red and processed meats, sugar, refined wheat, and saturated fats can contribute to inflammation, and such a diet is known as a pro-inflammatory diet [17]. A pro-inflammatory diet, as measured by higher Dietary Inflammatory Index (DII) scores, has been linked to both systemic low-grade inflammation and an increased risk of malignancies such as prostate, breast, colorectal, lung, and pancreatic cancer [18].

Inflammatory mediators, for example, CRP and IL-6, have been associated with increased risk of some cancer types [19]. Studies also showed that people with lower central adiposity who ate a more proinflammatory diet—a diet with higher intakes of salt, sugar, and saturated fat—had higher levels of pro-inflammatory gene expression compared to anti-inflammatory diet eaters [20]. Similarly, higher levels of CRP, IL-6, and fibrinogen are linked to the Western diet, which is high in red meat, high-fat dairy products, and refined carbohydrates [21-22]. Contrarily, a Mediterranean diet low in red meat and butter, high in whole grains, fruit, and green vegetables, along with moderate alcohol use, is linked to reduced levels of inflammation [23].

This study aims to describe how the inflammatory potential of the diet can be measured and to provide an overview of the epidemiologic studies currently available that investigated pro-inflammatory diet in relation to CRC and BC risk. Finally, this report will provide suggestions for future epidemiologic research on this topic.

Methods

A literature search of the MEDLINE database via PubMed was conducted with the use of the following exposure search terms in all fields: [dietary inflammatory index] OR [DII] OR [empirical dietary inflammatory index] OR [EDII]OR [Pro-inflammatory Diet] in combination with each of the following outcome terms: [colon cancer] OR [rectal cancer] OR [colorectal cancer] OR [colorectal adenoma] OR [colon adenoma] OR [colon neoplasm] OR [colorectal neoplasm]. The same exposure search terms were used for the following outcome terms: [urinary bladder cancer] OR [urinary bladder tumors] OR [urothelial cancer] OR [urothelial neoplasm]. Search results were limited to human epidemiological research published in English up to October 2022. Studies using dietary index scores, such as the DII and EDII, which represent the inflammatory potential of a person's diet, and that reported the estimated associations of interest, such as ORs, HRs, or RRs, and 95% CIs, were eligible and included for review. Information on the first author, year, country, study population, sample size, number of cases, sources of controls, a dietary assessment tool used, evaluation period, main effect result, and confounding variables corrected in the analysis was reported for each selected study.

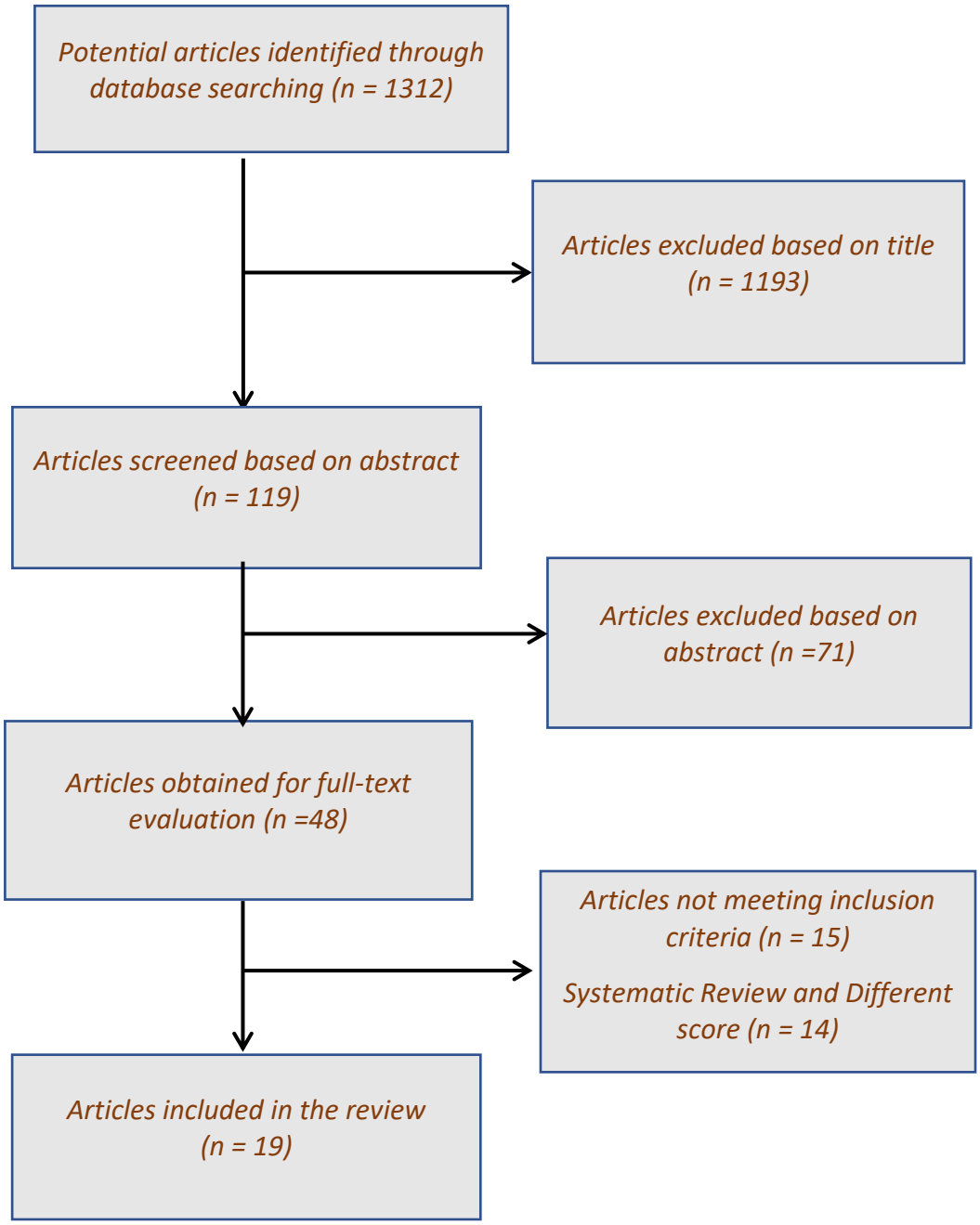

Figure.1. Flow chart and process selection of relevant studies exploring the association between pro-inflammatory diet and the risk of colorectal and bladder cancer.

Measurement of Inflammatory Potential of Diet

Dietary Inflammatory Index

The Dietary Inflammatory Index (DII®), which is composed mainly of nutrients, is a literature-based dietary score that was developed to measure the potential impact of a diet on the inflammatory status of an individual. A high DII score reflects the pro-inflammatory potential of the diet, whereas a low DII score reflects the anti-inflammatory potential of the diet. The overall inflammatory potential of a person's diet is indicated by the Dietary Inflammatory Index (DII). The DII ranges from −9 (most anti-inflammatory) to +8 (most pro-inflammatory) [24].

As described in Figure 1, after a thorough literature search, one of the three possible values was assigned to each article based on the effect of the food parameter on inflammation. The 'food parameter-specific overall inflammatory effect score' was then calculated by: (i) dividing the weighted pro- and anti-inflammatory articles by the total weighted number of articles and (ii) subtracting the anti-inflammatory fraction from the pro-inflammatory fraction. The current DII was standardized to a representative range of dietary intake based on actual human consumption. This was accomplished by constructing a composite database representing a wide range of diets across diverse populations living in a variety

of countries in different regions of the world. The DII includes common dietary elements like flavonoids, spices, and tea since it is based on research linking diet to inflammation and goes beyond micronutrients and macronutrients. Finally, calculation of the DII is based on dietary intake data that are then linked to the regionally representative world database that provide a robust estimate of a mean and standard deviation for each parameter [24].

The DII score was compared to inflammatory indicators such as C-reactive protein (CRP), IL-6, homocysteine, and fibrinogen. Higher DII scores are linked to increased circulating levels of inflammatory markers. Results based on continuous measures of CRP suggested that an increasing Inflammatory Index score (representing movement toward an anti-inflammatory diet) was associated with a decrease in CRP. The DII and the inflammatory indicator IL-6 exhibited substantial positive relationships in multivariable analyses, however no significant associations were seen between the DII and the inflammatory markers CRP and fibrinogen [25-26].

The Empirical Dietary Inflammatory Index

The Empirical Dietary Inflammatory Index (EDII), composed of food groups as reported on a food-frequency questionnaire (FFQ), is a hypothesis-driven, empirically determined dietary pattern that rates the quality of diets according to their propensity to cause inflammation. Dietary and inflammatory marker data in the Nurses'

Health Study (NHS) was used to develop the EDII. The construct validity of the EDII was evaluated in 2 independent samples of women and men in the Nurses' Health Study II (NHS-II) and the Health Professionals Follow-Up Study (HPFS). The goal for developing the EDII was to create an empirical score based on food groups to assess the overall inflammatory potential of whole diets [27]. An EDII composed of food groupsas reported on FFQ shows a greater ability to predict concentrations of plasma inflammatory markers than the DII [28].

Results

Pro-Inflammatory Diet and Risk of CRC

Case-control studies.

Results from ten case-control studies and four prospective cohort studies regarding association between a pro-inflammatory diet and the risk of CRC are summarized in Table 3. Ten case-control studies using either DII or EDII score all reported a positive association between a pro-inflammatory diet and CRC risk. A population-based case-control study conducted in Canada, concluded that proinflammatory diets were associated with an increased risk for CRC in the NL population. Significant associations were observed between the DII score and risk for CRC (OR continuous 1.10, 95%CI 1.01–1.20 and OR quartile 4 versus 1 1.65, 95%CI 1.13–2.42 [29].

A case-control in an Iranian population indicated a higher risk of CRC with an increase in DII score while using DII both as a continuous variable (OR continuous = 2.20,

95% CI: 1.22-3.87) and as a categorical variable (OR tertile 3 vs tertile1 = 2.47, 95%CI: 1.10-5.55). The main covariates that were taken into account were [30]. Similarly, in a case-control study done by Young et al, where 632 colorectal cancer patients and 1,295 healthy controls were included in the final analysis. Risk for CRC was positively associated with pro-inflammatory diet having OR 1.38(1.12-1.71) higher vs lower group of DII [31].

A case-control study done on data from the Bellvitge Colorectal Cancer Study identified a direct link between DII score and CRC risk (ORQ4 vs. Q1 1.65, 95%CI 1.05–2.60, and P trend 0.011), with a stronger association for colon cancer risk (ORQ4 vs. Q1 2.24, 95%CI 1.33–3.77, and P trend 0.002) than rectal cancer risk (ORQ4 vs. Q1 1.12, 95%CI 0.61–2.06, and P trend 0.37) [32]. A Jordanian study found that subjects with higher DII scores were at increased odds of CRC, with the DII being used both as a continuous variable (OR continuous =1.45, 95%CI: 1.13, 1.85; one-unit increase corresponding to ≈20% of its range in the current study) and as a categorical variable (OR tertile 3 vs tertile1 = 2.13, 95%CI: 1.23-3.72) [33].

Results of a case-control study in Argentina show that odds of colorectal cancer increased linearly with increasing DII scores (OR continuous 1.34; 95%CI 1.07 to 1.69 and ORtertile3 vs. tertile1 1.21; 95%CI 1.01 to 1.44). The association was stronger among men than women (OR continuous 1.29; 95%CI 1.21 to 1.37 vs. OR continuous 1.05; 95%CI 0.83 to 1.33, respectively) [34].

Likewise, in MCC-Spain-Study EDII was associated with colorectal cancer risk (OR = 1.93, highest quartile versus lowest, 95%CI:1.60–2.32; p-trend: <0.001); this increase was observed for both colon and rectal cancer [35]. In a multi-center case-control study conducted between 1992 and 1996 in Italy, higher DII scores (i.e., with a more pro-inflammatory diet) had a higher risk of CRC, with the DII being used both as a continuous variable and as a categorical variable [36]. A study carried out between August 2010 and August 2013 at the Centre for Colorectal Cancer of the National Cancer Centre in Korea on cases and controls of the same center found a higher DII score (representing a more pro-inflammatory diet) was associated with an increased incidence of colorectal cancer (OR (95% CI) = 2.16 (1.71, 2.73) for highest vs. lowest tertile [37]. Finally, a case-control study was carried out to investigate whether the dietary inflammatory index (DII) is associated with the risk of colorectal cancer in the Chinese population. Also, here the DII was associated with colorectal cancer risk, with the OR= 1.40 (95% CI1.16,1.68; Ptrend 0.01) for the highest DII quartile compared to the lowest quartile [38].

Cohort studies.

Four cohort studies also found a positive association between a pro-inflammatory diet and CRC risk. A prospective study in the Women's Health Initiative including a total of 1,920 cases of CRC revealed that consuming pro-inflammatory foods is linked to a higher risk of CRC, particularly malignancies of the proximal colon. Higher DII scores were associated with an increased

incidence of overall CRC (HR- Q5 vs Q1 1.22; 95%CI 1.05, 1.43; p trend = 0.02) and colon cancer, specifically proximal colon cancer (HR-Q5 vs Q1 1.35; 95%CI 1.05, 1.67; p trend = 0.01) but not distal colon cancer [39]. The Iowa Women's Health Study including 1,636 incident colorectal cancers, including 1,329 colon and 325 rectal cancers. Authors found that a pro-inflammatory diet, indicated by a higher DII score, was associated with an increased risk of CRC (HR for DIIcontinuous: 1.07 per unit increase in DII (corresponding to 0.5 SD unit increase); 95% confidence interval (CI), 1.01–1.13; HR for DIIquintiles: Q5 vs. Q1 = 1.20; 95%CI, 1.01–1.43) [40].

Using participants from the National Institutes of Health-American Associations of Retired Persons Diet and Health Study, overall CRC risk was higher in DII quartile 4 compared to quartile 1 (HR 1.40, 95%CI 1.28-1.53; P for trend 0:01) [41]. In the multi-ethnic cohort study done by Harmon et al a more proinflammatory diet (quartile 4 compared to quartile1) was linked to an elevated risk of overall CRC risk (HR 1.21, 95%CI 1.11-1.32; P-trend0.01) [42].

TABLE 3. SUMMARY OF EPIDEMIOLOGICAL STUDIES EXAMINING THE ASSOCIATION OF A PRO-INFLAMMATORY DIET AND CRC RISK					
STUDY	**Study Type**	**Sample size**	**Dietary score**	**Outcome**	**Adjusted confounders**
SHIVAPPA ET AL. 2015 ITALY [36]	Case-control study	Cases = 1953 Hospital based Controls = 4154	DII	OR continuous = 1·13, 95%CI: 1·09- 1·18 OR Q5 vs Q1 = 1·55, 95%CI: 1·29-1·85	age, sex, study centre, education, BMI, alcohol drinking, physical activity, and family history of CRC
ZAMORA-ROS ET AL. 2015 SPAIN [35]	Case-control study	Cases = 424 Hospital based Controls = 401	DII	OR Q4 vs. Q1 = 1.65, 95%CI: 1.05–2.60	BMI, physical activity, NSAIDs/aspirin use, and tobacco smoking
YOUNG ET AL. 2016 KOREA [37]	Case-control study	Cases = 923 Hospital based Controls = 1846	DII	OR = 2.16, 95%CI: 1.71- 2.73 (for highest vs. lowest tertile)	
ISHOR ET AL. 2017 CANADA [29]	Case-control study	Cases = 547 Population based	DII	OR continuous = 1.10, 95%CI: 1.01–1.20	age, sex, BMI, physical activity, cholesterol level, triacylglycerols (TGs),

		control = 685		OR Q4 vs Q1 = 1.65 95%CI: 1.13–2.42	family history of CRC, polyps, diabetes, history of colon screening, cigarette smoking, alcohol consumption, NSAIDs
SHIVAPPA ET AL. 2017 JORDAN [33]	Case-control study	Cases = 153 Control = 202 subjects' frequency matched on age, sex, and occupation	DII	OR continuous =1.45, 95%CI: 1.13-1.85 OR tertile 3 vs tertile1 = 2.13 95%CI: 1.23-3.72	age, sex, education, physical activity, BMI, smoking, and family history of CRC.
SHIVAPPA ET AL. 2018 IRAN [30]	Case-Control study	Cases = 72 Hospital based Controls = 142	DII	OR continuous = 2.20, 95%CI: 1.22-3.87 OR tertile 3 vs tertile1 = 2.47, 95%CI: 1.10 5.55	age, sex, education, energy intake, exercise, BMI, smoking, family history of cancer, and history of aspirin, acetaminophen, and multivitamin used

NICLIS ET AL. 2018 ARGENTINA [34]	Case-control study	Cases = 144 Controls = 302	DII	OR continuous = 1.34, 95%CI 1.07-1.69 OR tertile3 vs tertile1= 1.21, 95%CI 1.01-1.44	age, BMI, sex, calorie intake, smoking habits, socioeconomic position, degree of physical activity, and usage of nonsteroidal anti-inflammatory medicines
SANTACANA ET AL. 2019 SPAIN [32]	Case-control study	Cases = 1852 Population based Controls = 3437	EDII	ORQ4 vs Q1 = 1.65, 95%CI:1.05-2.60	sex, age, educational level, study area, family history of colorectal cancer, tobacco smoking, physical activity, BMI, and NSAIDs/aspirin use
YOUNG ET AL. 2019 KOREA [31]	Case-control study	Cases = 632 Hospital based Controls = 1295	DII	OR = 1.38, 95%CI: 1.12-1.71	age, sex, family history of colorectal cancer, education, obesity, physical activity, smoking, alcohol consumption, and dietary inflammatory index

ABULIMITI ET AL. 2020 CHINA [38]	Case-control study	Cases = 2502 Hospital based Controls = 2538	DII	OR = 1.40 (highest quartile vs lowest) 95%CI: 1.16- 1.68	age, sex, marital status, residence, educational level, occupation, income, BMI, smoking status, alcohol drinking, first degree relative with cancer, history of diabetes mellitus, occupational activity, household and leisure-time activities
HARMON ET AL. 2014 USA [42]	Prospective cohort study	N = 489 422 CRC incident = 6944	DII	HR = 1·40, 95%CI: 1·28- 1·53	Age, sex, race, diabetes, asthma, use of supplements, smoking status, family history of colon cancer, education, hormone (i.e., oestrogen or progesterone) use, aspirin use and BMI

SHIVAPPA ET AL. 2014 MINNESOTA USA [40]	Prospective cohort study	N = 34,703 CRC incident = 1,636	DII	HR DII continuous = 1.07 95%CI: 1.01-1.13 HR Q5vsQ1=1.20 95%CI: 1.01-1.43	BMI, smoking status, pack-years of smoking, hormone replacement therapy, education, diabetes, and total energy intake
TABUNG ET AL. 2015 USA [39]	Prospective cohort study	152,536 women aged 50–79 years without CRC. CRC incident = 1,920	DII	HR Q5 vs Q1 = 1.22 95%CI: 1.05-1.43 Proximal colon cancer HRQ5 vs Q1 = 1.35 95%CI 1.05-1.67	age, total energy intake, BMI, race/ethnicity, physical activity, educational level, smoking status, family history of colorectal cancer, hypertension, diabetes, arthritis, colonoscopy, history of occult blood tests, NSAID
BROOK, ET AL. 2017 TENNESSEE USA [41]	Prospective study	N = 190,963	DII	quartile 4 compared to quartile 1 HR = 1.40, 95%CI 1.28-1.53)	N/A

Pro-Inflammatory Diet and Risk of BC

Case-control studies

Results from three prospective and two case-control studies regarding the potential of a pro-inflammatory diet and the risk of urinary bladder cancer are summarized in Table 4. A case-control investigation carried out in Italy between 2003 and 2014 concluded that a pro-inflammatory diet as indicated by higher DII scores is associated with increased BC risk where subjects in the highest quartile of DII scores (i.e., with a more pro-inflammatory diet) had a higher risk of BC compared to subjects in the lowest quartile (i.e., with an anti-inflammatory diet) (ORQuartile4vs1 = 1.97; 95% [confidence interval], 1.28, 3.03; P trend = .003) [43].

A case-control study conducted in the Iranian population demonstrated that subjects with higher DII score (>–0.12) are at higher risk of bladder cancer [odds ratio (OR) = 2.46; 95% CI = 1.12–5.41, P value = 0.02)] compared to subjects with lower DII scores (≤–0.12) [44].

Cohort studies.

Over a median follow-up of 12.5 years among 101,721 participants in the Prostate, Lung, Colorectal, and Ovarian (PLCO) study 776 BC incident occurred, authors showed no association between E-DII and bladder cancer risk in the multivariable models. For both men and women, the HRs (95% CIs) in the highest versus lowest EDII quintile were 0.90(0.70-1.17) and 1.22(0.72-2.06), respectively [45].

In another prospective study, over a median follow-up time of 21.3 years, none of the dietary scores was associated with the increased risk of UCC overall [46]. Using EDII score, the result of three United States

prospective cohort studies revealed high EDII scores that suggest dietary habits that may cause inflammation were not linked to an increased risk of bladder cancer (quintile 5 vs 1 pooled multivariable adjusted RR 0.92, 95% CI 0.75–1.12, ptrend = 0.67) [47].

TABLE 4. SUMMARY OF MAJOR EPIDEMIOLOGICAL STUDIES EXAMINING THE ASSOCIATION OF PRO-INFLAMMATORY DIET AND BC RISK

STUDY	Study type	Sample size	Dietary Score	Outcome	Adjusted confounders
SHIVAPPA ET AL. 2017 ITALY [43]	Case-Control study	Cases = 56 Hospital base Controls = 109	DII	Higher vs lower DII score OR = 2.46, 95%CI = 1.12–5.41	age, sex, total energy intake, BMI, smoking, alcohol intake
HÉBERT ET AL. 2019 IRAN [44]	Case-Control study	Cases= 690 Hospital	DII	Highest quartile vs lowest quartile DII	age, sex, BMI physical

		base Controls =665		score OR = 1.08, 95%CI= 1.00–1.17	activity, smoking status, alcohol use, and family history of cancer
DUGUÉ ET AL. 2016 AUSTRALIA, MELBOURNE COLLABORATIVE COHORT STUDY (MCCS) [46]	Prospective Cohort study	Participants, The Melbourne Collaborative Cohort Study (MCCS) = 41514 UCC cases = 379	DII	DII score Q5 vs Q1 HR = 1.06, 95%CI: 0.96–1.18	sex, country of birth, smoking, alcohol consumption, body mass index physical activity, education, and socioecono

					mic status
ABUFARAJ ET AL. 2019 USA, NURSES' HEALTH STUDY [47]	Prospective Cohort Studies	N = 172,802 BC incident = 1,042	EDII	Q5 vs Q1 RR = 0.92, 95%CI: 0.75–1.12	N/A
JINDAN LUO ET AL. 2020 USA, PLCO STUDY [45]	Prospective study	N = 101,721 BC incident = 776	DII	Highest vs lowest HR = 0.90, 95%CI: 0.70–1.17	Smoking, sex, BMI, family history

Discussion

provoke acute inflammation which leads to carbonification and ultimately cancer of the

This review summarizes existing research on the relationship between a pro-inflammatory diet, as measured by DII or EDII CRC, and the risk of CRC and BC. We showed that there is a strong positive association between a pro-inflammatory diet and risk of CRC, however, association between a pro-inflammatory diet and risk of BC is not evident.

Regarding the association between a pro-inflammatory diet, and the risk of colorectal cancer, our results are in line with a previous meta-analysis published in 2017 that demonstrated an increased risk was related to a higher DII score [48]. Nine articles were included in that quantitative meta-analysis which is less than our included number of articles. With a total number of fourteen, we included ten case-control studies and four prospective cohort studies. Contrary to this, our finding shows that a diet high in proinflammatory factors or low in anti-inflammatory factors was not related to a higher risk of developing BC, as has also been reported in another systematic review and meta-analysis on dietary patterns and risk of bladder cancer [49]. In the mentioned systematic review and meta-analysis, the authors included more research articles (n= 12) on the subject than our review (n= 5). They also looked at other dietary scores such as Western diet and Mediterranean diet and they found positive and negative association between the two-diet score and risk of BC, respectively.

The ten case-control studies on the association between a pro-inflammatory diet and the risk of CRC in this review tended to report larger effect estimates, compared to four cohort studies. This might be due to recall bias in case-control studies [50], which might skew results away from the null if medical status influences recall of cases differently than controls. Loss to follow-up or similarity of the research population in cohort studies, which might attenuate results toward the null. In cohort studies, we found no significant association between a pro-inflammatory diet and BC risk. In case-control studies, however, a strong direct association between a pro-inflammatory diet and BC was discovered. A strong positive association between pro-inflammatory diet and risk of CRC compare to BC might be due to the fact that pro-inflammatory factors are constantly or for more time in contact with mucosal lining of the bowel may bowel.

The effect of a pro-inflammatory diet on insulin resistance through raising systemic inflammation is one of the most frequently taken into consideration of the many theories that explain the connection between the pro-inflammatory diet and CRC and BC risk [51]. Inflammation is not the only route through which dietary variables are linked to CRC and BC. For instant, consuming red and processed meat raises the risk of CRC due to higher amounts of haem iron concentration [52].

This review had a number of strengths. Studies that were part of this review tended to use study design techniques like matching or statistical adjustments to control for acceptable confounders. Every study adjusted for age, sex (where applicable), and BMI or obesity status. The majority of research also took into account factors like smoking status, overall calorie consumption, physical activity, and family history of CRC while few also took into consideration the use of NSAIDs. Studies on the association between a pro-inflammatory diet and the risk of CRC have been done on multiple ethnic groups and on the population of multiple countries which shows generalizability.

This literature review had some limitations. First, all studies' DII or EDII scores were based on participants' self-reports using food frequency questionnaires, which might not always provide accurate information. We believe that recall bias affects self-assessments made with these tools in case-control studies, which may result in a

misrepresentation of the exposure. Second, dietary changes may occur during the study's follow-up period in cohort studies when the DII or EDII score was assessed at the start. However, adult dietary patterns can be considered to remain largely constant across time [53]. Another limitation of the review included the diverse nature of the selected articles based on study population characteristic, sample size, follow-up periods and study design. Nevertheless, each study's inherent confounding variables and limited sample size in some studies contribute to the limitations that could influence the results.

Conclusions and future directions

There is much and consistent epidemiological studies, from diverse population groups, suggesting the positive association between a pro-inflammatory diet and risk of colorectal cancer. However, epidemiological research on the relationship between a pro-inflammatory diet and the risk of urinary bladder cancer is few and contradictory. Our study shows that dietary patterns might play a crucial role in CRC prevention and therefor public health authorities pay more attention to recommend consumption of diet that contain more anti-inflammatory factors and decrease diet that contain more pro-inflammatory factors.

Future research involving pragmatic clinical trials on pro-inflammatory diet, if possible, and plan for preventive intervention strategies needed. On the other hand, to rule out significant positive or negative association between a pro-inflammatory diet and risk of BC, more robust Epidemiological studies involving multi-ethnic population are needed.

References

1. Lotfollahzadeh, S., Recio-Boiles, A., & Cagir, B. (2022). Colon Cancer. In StatPearls. StatPearls Publishing.
2. Mattiuzzi, C., et al. (2019). Concise update on colorectal cancer epidemiology. Annals of translational medicine, 7(21), 609. https://doi.org/10.21037/atm.2019.07.91
3. Li, N., et al. (2021). Incidence, mortality, survival, risk factor and screening of colorectal cancer: A comparison among China, Europe, and northern America. Cancer letters, 522, 255–268. https://doi.org/10.1016/j.canlet.2021.09.034
4. Friedenreich, C. M., et al. (2021). Physical activity, obesity and sedentary behavior in cancer etiology: epidemiologic evidence and biologic mechanisms. Molecular oncology, 15(3), 790–800. https://doi.org/10.1002/1878-0261.12772
5. Oyeyemi, S.O., Braaten, T., Licaj, I. et al. Physical activity patterns and the risk of colorectal cancer in the Norwegian Women and Cancer study: a population-based prospective study. BMC Cancer 18, 1216 (2018). https://doi.org/10.1186/s12885-018-5092-0
6. Hannan, L. M., et al. (2009). The association between cigarette smoking and risk of colorectal cancer in a large prospective cohort from the United States. Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 18(12), 3362–3367. https://doi.org/10.1158/1055-9965.EPI-09-0661
7. Bray, F., et al. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 68(6), 394–424. https://doi.org/10.3322/caac.21492

8. Zeegers, M. P., et al. (2000). The impact of characteristics of cigarette smoking on urinary tract cancer risk: a meta-analysis of epidemiologic studies. Cancer, 89(3), 630–639. https://doi.org/10.1002/1097-0142(20000801)89:3<630::aid-cncr19>3.3.co;2-h

9. International Agency for Research on Cancer. (1993). Occupational exposures of hairdressers and barbers and personal use of hair colourants; some hair dyes, cosmetic colourants, industrial dyestuffs and aromatic amines. IARC monographs on the evaluation of carcinogenic risks to humans, 57.

10. Hodder, S. L., et al. (2000). Predisposition to urinary tract epithelial metaplasia in Schistosoma haematobium infection. The American journal of tropical medicine and hygiene, 63(3-4), 133–138. https://doi.org/10.4269/ajtmh.2000.63.133

11. Li, F., An, S., Hou, L., Chen, P., Lei, C., & Tan, W. (2014). Red and processed meat intake and risk of bladder cancer: a meta-analysis. International journal of clinical and experimental medicine, 7(8), 2100–2110.

12. Barry, K. H. et al (2020). Ingested Nitrate and Nitrite and Bladder Cancer in Northern New England. Epidemiology (Cambridge, Mass.), 31(1), 136–144. https://doi.org/10.1097/EDE.0000000000001112

13. Tabung, F. K., et al. (2018). An empirical dietary inflammatory pattern score is associated with circulating inflammatory biomarkers in a multi-ethnic population of postmenopausal women in the United States. The Journal of nutrition, 148(5), 771-780.

14. Friis, S., et al. (2015). Low-Dose Aspirin or Nonsteroidal Anti-inflammatory Drug Use and Colorectal Cancer Risk: A Population-Based, Case-Control Study. Annals of internal medicine, 163(5), 347–355. https://doi.org/10.7326/M15-0039

15. Gakis, G. (2014). The role of inflammation in bladder cancer. Inflammation and Cancer, 183-196.

16. Panickar, K. S., & Jewell, D. E. (2015). The beneficial role of anti-inflammatory dietary ingredients in attenuating markers of chronic low-grade inflammation in aging. Hormone molecular biology and clinical investigation, 23(2), 59–70. https://doi.org/10.1515/hmbci-2015-0017

17. Belliveau, R., et al. (2022). Pro-inflammatory diet and depressive symptoms in the healthcare setting. BMC psychiatry, 22(1), 1-7.

18. Bodén, S., et al. (2019). The inflammatory potential of diet in determining cancer risk; A prospective investigation of two dietary pattern scores. PloS one, 14(4), e0214551. https://doi.org/10.1371/journal.pone.0214551

19. Heikkilä, K., et al. (2009). Associations of circulating C-reactive protein and interleukin-6 with cancer risk: findings from two prospective cohorts and a meta-analysis. Cancer causes & control: CCC, 20(1), 15–26. https://doi.org/10.1007/s10552-008-9212-

20. Padin, A. C., et al. (2019). A proinflammatory diet is associated with inflammatory gene expression

among healthy, non-obese adults: Can social ties protect against the risks? Brain, behavior, and immunity, 82, 36–44. https://doi.org/10.1016/j.bbi.2019.07.031

21. Johansson-Persson, et al. (2014). A high intake of dietary fiber influences C-reactive protein and fibrinogen, but not glucose and lipid metabolism, in mildly hypercholesterolemic subjects. European journal of nutrition, 53(1), 39–48. https://doi.org/10.1007/s00394-013-0496-8

22. King, D. E., Egan, B. M., & Geesey, M. E. (2003). Relation of dietary fat and fiber to elevation of C-reactive protein. The American journal of cardiology, 92(11), 1335–1339. https://doi.org/10.1016/j.amjcard.2003.08.020

23. Estruch, R. et al., & PREDIMED Study Investigators (2006). Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. Annals of internal medicine, 145(1), 1–11. https://doi.org/10.7326/0003-4819-145-1-200607040-00004

24. Shivappa, N., et al. (2014). Designing and developing a literature-derived, population-based dietary inflammatory index. Public health nutrition, 17(8), 1689–1696. https://doi.org/10.1017/S1368980013002115

25. Cavicchia, P.et al (2009). A new dietary inflammatory index predicts interval changes in serum high-sensitivity C-reactive protein. The Journal of nutrition, 139(12), 2365–2372. https://doi.org/10.3945/jn.109.114025

26. Shivappa, N., et al. (2015). Associations between dietary inflammatory index and inflammatory markers in the Asklepios Study. The British journal of nutrition, 113(4), 665–671. https://doi.org/10.1017/S000711451400395X

27. Tabung, F. et al (2016). Development and Validation of an Empirical Dietary Inflammatory Index. The Journal of nutrition, 146(8), 1560–1570. https://doi.org/10.3945/jn.115.228718

28. Tabung, F. K, at al (2017). An Empirical Dietary Inflammatory Pattern Score Enhances Prediction of Circulating Inflammatory Biomarkers in Adults. The Journal of nutrition, 147(8), 1567–1577. https://doi.org/10.3945/jn.117.248377

29. Sharma, I., Zhu, Y., Woodrow, J. R. et al. (2017). Inflammatory diet and risk for colorectal cancer: A population-based case-control study in Newfoundland, Canada. Nutrition (Burbank, Los Angeles County, Calif.), 42, 69–74. https://doi.org/10.1016/j.nut.2017.05.010

30. Shivappa, N., et al. (2018). Dietary Inflammatory Index and Odds of Colorectal Cancer in a Case- Control Study from Iran. Asian Pacific journal of cancer prevention: APJCP, 19(7), 1999–2006. https://doi.org/10.22034/APJCP.2018.19.7.1999

31. Cho, Y. A., et al. (2019). Genetic Risk Score, Combined Lifestyle Factors and Risk of Colorectal Cancer. Cancer research and treatment, 51(3), 1033–1040. https://doi.org/10.4143/crt.2018.447

32. Obón-Santacana, et al. (2019). Dietary Inflammatory Index, Dietary Non-Enzymatic Antioxidant Capacity, and Colorectal and Breast Cancer Risk (MCC-Spain Study). Nutrients, 11(6), 1406. https://doi.org/10.3390/nu11061406

33. Shivappa, N., et al. (2017). Dietary inflammatory index and odds of colorectal cancer in a case-control study from Jordan. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme, 42(7), 744–749. https://doi.org/10.1139/apnm-2017-0035

34. Niclis, C., et al. (2018). Proinflammatory Dietary Intake is Associated with Increased Risk of Colorectal Cancer: Results of a Case-Control Study in Argentina Using a Multilevel Modeling Approach. Nutrition and cancer, 70(1), 61–68. https://doi.org/10.1080/01635581.2018.1397710

35. Obón-Santacana, V., et al. (2019). Dietary Inflammatory Index, Dietary Non-Enzymatic Antioxidant Capacity, and Colorectal and Breast Cancer Risk (MCC-Spain Study). Nutrients, 11(6), 1406. https://doi.org/10.3390/nu11061406

36. Shivappa, N., et al. (2015). Inflammatory potential of diet and risk of colorectal cancer: a case-control study from Italy. The British journal of nutrition, 114(1), 152–158. https://doi.org/10.1017/S0007114515001828

37. Cho, Y. A., et al. (2016). Dietary Inflammatory Index and Risk of Colorectal Cancer: A Case-Control Study in Korea. Nutrients, 8(8), 469. https://doi.org/10.3390/nu8080469

38. Abulimiti, A., Zha & Zhang, C. X et al. (2020). The Dietary Inflammatory Index Is Positively Associated with Colorectal Cancer Risk in a Chinese Case-Control Study. Nutrients, 12(1), 232. https://doi.org/10.3390/nu12010232

39. Tabung, F. K., Et al (2015). The association between dietary inflammatory index and risk of colorectal cancer among postmenopausal women: results from the Women's Health Initiative. Cancer causes & control: CCC, 26(3), 399–408. https://doi.org/10.1007/s10552-014-0515-y

40. Shivappa, N., Prizment, A. E., et al (2014). Dietary inflammatory index and risk of colorectal cancer in the Iowa Women's Health Study. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 23(11), 2383–2392. https://doi.org/10.1158/1055-9965.EPI-14-0537

41. Wirth, M. D., Burch, J., & Hébert, J. R et al. (2014). Association of a dietary inflammatory index with inflammatory indices and metabolic syndrome among police officers. Journal of occupational and environmental medicine, 56(9), 986–989. https://doi.org/10.1097/JOM.0000000000000213

42. Harmon BE, Hébert JR et al. The Dietary Inflammatory Index Is Associated with Colorectal Cancer Risk in the Multiethnic Cohort. J Nutr. 2017 Mar;147(3):430-438. doi: 10.3945/jn.116.242529. Epub 2017 Feb 8. PMID: 28179489; PMCID: PMC5320401

43. Shivappa, N., Hébert, J. R., Rosato, V., Rossi, M, et al. (2017). Dietary

Inflammatory Index and Risk of Bladder Cancer in a Large Italian Case-control Study. Urology, 100, 84–89. https://doi.org/10.1016/j.urology.2016.09.026

44. Shivappa, N., Hébert, J. R., Mirsafa, F., & Rashid Khani, B. (2019). Increased Inflammatory Potential of Diet Is Associated with Increased Risk of Bladder Cancer in an Iranian Case-Control Study. Nutrition and cancer, 71(7), 1086–1093. https://doi.org/10.1080/01635581.2019.1597902

45. Luo, J., Shivappa, N., Hébert, J. R., & Xu, X. (2020). Dietary inflammatory index and bladder cancer risk: a prospective study. European journal of clinical nutrition, 74(10), 1428–1433. https://doi.org/10.1038/s41430-020-0602-y

46. Dugué, P. A., Hodge, A. M., & Giles, G. G et al. (2016). Association between selected dietary scores and the risk of urothelial cell carcinoma: A prospective cohort study. International journal of cancer, 139(6), 1251–1260. https://doi.org/10.1002/ijc.30175

47. Abufaraj, M., Tabung, F. K., & Schernhammer, E et al. (2019). Association between Inflammatory Potential of Diet and Bladder Cancer Risk: Results of 3 United States Prospective Cohort Studies. The Journal of urology, 202(3), 484–489. https://doi.org/10.1097/JU.0000000000000279

48. Shivappa, N., et al. (2017). Dietary Inflammatory Index and Colorectal Cancer Risk-A Meta-Analysis. Nutrients, 9(9), 1043. https://doi.org/10.3390/nu9091043

49. Dianatinasab, M., et al. (2022). Dietary patterns and risk of bladder cancer: a systematic review and meta-analysis. BMC public health, 22(1), 73. https://doi.org/10.1186/s12889-022-12516-2

50. Chouinard, E., & Walter, S. (1995). Recall bias in case-control studies: an empirical analysis and theoretical framework. Journal of clinical epidemiology, 48(2), 245–254. https://doi.org/10.1016/0895-4356(94)00132-a

51. Festa, A., et al. (2000). Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). Circulation, 102(1), 42–47. https://doi.org/10.1161/01.cir.102.1.42

52. Gilsing, A. M., et al. (2013). Dietary heme iron and the risk of colorectal cancer with specific mutations in KRAS and APC. *Carcinogenesis*, *34*(12), 2757–2766. https://doi.org/10.1093/carcin/bgt290

53. Thompson, F. E., et al. (1990). Characteristics of individuals and long-term reproducibility of dietary reports: the Tecumseh Diet Methodology Study. Journal of clinical epidemiology, 43(11), 1169–1178. https://doi.org/10.1016/0895-4356(90)90018-

54. Weng, H., et al. (2017). Tea Consumption and Risk of Bladder Cancer: A Dose-Response Meta-Analysis. Frontiers in physiology, 7, 693. https://doi.org/10.3389/fphys.2016.00693

55. https://www.wcrf.org/wp-content/uploads/2021/02/Bladder-cancer-report.pdf