Vitamin B1 Intake and the Risk of Colorectal Cancer: a Systematic Review of Observational Studies

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Summary Colorectal cancer is the main leading cause of death from cancer worldwide. Protective effects of vitamin B1 on colorectal cancer have been observed in some epidemiological studies. A systematic review and meta-analysis of observational studies evaluated the association of intake of vitamin B1 with the incidence of colorectal cancer. Relevant studies were identified in MEDLINE via PubMed (published up to September 2020). We extracted data from articles on vitamin B1 and used a multivariable-adjusted odds ratio (OR) and a random-effects model for analysis. We found seven articles meeting the inclusion criteria (1 of cohort studies and 6 case-control studies) and a total of 6,184 colorectal cancer cases were included in this meta-analysis. The multivariable-adjusted OR for pooled studies for the association of roughly the same high dose level versus the lowest vitamin B1 intake and the risk of colorectal cancer was 0.76 (95% confidence interval (95% CI): 0.65, 0.89). This meta-analysis studied the relationship between vitamin B1 and colorectal cancer. We found vitamin B1 intake was inversely associated with the risk of colorectal cancer. However, further research and large sample studies need to be conducted to better validate the result.

Key Words colorectal cancer, vitamin B1, risk, thiamin, meta-analysis

According to Global Cancer Statistics 2018, colorectal cancer ranks third in terms of incidence but second in terms of mortality. Over 1.8 million new colorectal cancer cases and 881,000 deaths are estimated to occur in 2018. The highest colon cancer incidence rates are found in parts of Europe, Australia/New Zealand, Northern America, and Eastern Asia (1). Age, genetic and environmental factors play a major role in the development of colorectal cancer. Much research has suggested that nutrition may play both a causal and protective role in the development of colon cancer. Dietary composition (2), obesity, and lack of physical activity are established contributors to the risk of colorectal cancer, but the underlying causative biological processes are not determined (3).

Vitamin B1 (thiamin), is a water-soluble vitamin critical for the proper function of most tissues and organs due to its pivotal role in carbohydrate and amino acid catabolism and gluconeogenesis (4). Some investigations of the relationship between various types of cancer and supplemental vitamins gradually increase. Vitamin supplements can reduce the incidence of cancer, some study suggests that there may be an inverse relationship between serum vitamin D levels and the risk of liver cancer (5, 6). Low levels of thiamine in the serum will increase cancer incidence. According to genetic research, the stomach is one of the major organs responsible for the absorption of thiamine. SLC19A3, one of the thiamin carriers, is a candidate tumor suppressor gene in gastric cancer (7). Genetic studies have shown that SLC19A1 gene, transcription factor p53, transketolase, NOX (nitrogen oxide) and PARP (poly ADP-ribose polymerase) may associate thiamine with colorectal cancer. Non-genomic mechanisms, including protein expression, inflammation, oxidative stress, and cell metabolism (8).

As for the impact of thiamin on colorectal cancer, some studies have demonstrated that thiamin deficiency has been observed in patients with colorectal cancer. A study from Poland has shown that higher consumption of alcohol, when combined with a low intake of retinol, thiamine antioxidant micronutrients, increased the risk of colorectal cancer and established a cancer-preventive role for retinol and thiamine (9). A clinical trial showed that postoperative serum vitamin B1 levels were significantly lower than those before the operation in patients with gastrectomies, whereas there was no significant

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Abbreviations: 95%CI, 95% confidence interval; ACF, aberrant crypt foci; NOS, Newcastle-Ottawa Scale; NOX, nitrogen oxide; OR, Odds Ratio; PARP, poly ADP-ribose polymerase; RR, relative risk.
difference in serum vitamin B1 levels before and after the surgeries in patients with colorectal cancer (10).

Protective effects of Vitamin B1 on colorectal cancer have been observed in some epidemiological studies, while some studies showed no significant association between Vitamin B1 and colorectal cancer. Therefore, our article mainly used a systematic review and meta-analysis of observational studies assessing the association of intake of vitamin B1 and the incidence of colorectal cancer. This meta-analysis studied the relationship between vitamin B1 and colorectal cancer. Through our articles, which will provide the scientific basis for future prevention and treatment of colorectal cancer.

**MATERIALS AND METHODS**

**Literature search.** We searched for observational studies of colorectal cancer and vitamin B1 published up to September 2020 in PubMed. We used the following MeSH terms and free text words: (1) vitamin OR vitamin B1 OR thiamin OR thiamine OR aneurin OR antiberiberi factor OR thiamine chloride OR dietary intake OR diet OR nutritional intervention OR nutrition. (2) colorectal OR colorectum OR colon OR colonic OR rectal OR rectum) AND (neoplasm OR cancer OR adenocarcinoma OR carcinoma OR tumor OR tumor). (3) “prospective Studies”[Mesh] OR “cohort studies”[Mesh] OR “follow-up studies”[Mesh] OR “observational studies”[Mesh] OR “case-control studies”[Mesh] (11). Besides, we reviewed reference lists of retrieved reviews or meta-analyses to identify further studies (12).

**Study selection.** Studies were included if they met the following inclusion criteria: (1) the exposure of interest was vitamin B1 or thiamine intake (2) The main outcome was the incidence of colon, colorectal or rectal cancer (3) Study types were observational studies (case-control studies or cohort studies); (4) Odds ratio (OR) or relative risk (RR) with 95% confidence intervals (95%CI) were reported. We retained the article with the best quality if there are multiple publications of similar documents or the same study.

**Data extraction and quality assessment.** The final eligible articles were reviewed independently by three investigators and extracted in duplicate the following characteristics: the first author’s name; publication year; the location where the study was performed; follow up period; sample size (cases and controls or cohort size); subject age and sex; the range of consumption; NOS (Newcastle-Ottawa Scale) grade; variables adjusted in the analysis; measurement method. The main outcomes were RR or OR estimates with corresponding 95% CI for roughly the same high dose level versus lowest categories of intake. Decisions were made by consultation or consensus with a fourth investigator. If data from any of the above categories were not reported in the primary article, items were treated as “not reported”. For each eligible study, two reviewers independently performed a quality assessment in duplicate by using
Table 1. Characteristic of Included Studies and Quality Score.

| No. of Controls | NOS | Variables of adjustment | Vitamin B1 assessment | No. | Follow up period | Location | Age median (quintile) | Gender | No. of Controls (size of cohort) | Study characteristics |
|-----------------|-----|-------------------------|-----------------------|-----|-----------------|----------|----------------------|--------|-------------------------------|---------------------|
| 24              | 6   | F                       | FFQ (Interview)       | 283 | 1997–2004       | China    | 40–70                | F      | 73,031                       | Shin A et al.       |
| 1,116           | 6   | F                       | FFQ (Interview)       | 2,083 | 1991–1994     | USA      | 30–79                | F      | 2,476                        | Slattery ML et al.  |
| 0.96            | 7   | F                       | FFQ (Interview)       | 854  | 2005–2007       | Australia| 40–79                | F      | 958                          | Lee LV et al.       |
| 0.69            | 7   | F                       | FFQ (Interview)       | 1,953 | 1992–1996     | Italy    | 23–74                | M      | 4,154                        | La Vecchia C et al. |
| 1.54            | 7   | F                       | FFQ (Interview)       | 180  | 1998–1999       | Poland   | 30–79                | F      | 180                          | Jedrychowski W et al. |
| 1.28            | 7   | F                       | FFQ (Interview)       | 1,951 | 2005–2017     | UK       | 28–70                | F      | 1,951                        | Key TJ et al.       |
| 1.62            | 6   | F                       | FFQ (Interview)       | 505  | 2005–2017       | Canada   | 28–70                | F      | 3,107                        | Arthur RS et al.    |

The characteristics of the included studies are summarized in Table 1. The 7 articles of vitamin B1 (thiamine) intake and colorectal cancer There are 1 cohort studies and 6 case-control studies (1nested case-control study and 1 case-cohort study) in total. aBriefly, we reviewed 2,298 articles of vitamin or vitamin B1 or thiamine and risk of colorectal, colon, or rectal cancer published up to September 2020. We identified 7 articles of vitamin B1 (thiamine) intake and colorectal cancer. There are 1 cohort studies and 6 case-control studies (1nested case-control study and 1 case-cohort study) in total. Study characteristics

The characteristics of the included studies are summarized in Table 1. The 7 articles of vitamin B1 (6,184 cases, age range 23–79 y) were published between 1997–2019; each study was conducted in the USA (20), Australia (21), Italy (22), Poland (23), China (24), UK (25), Canadians (26). The subjects of one study were female, and subjects of four were both female and male. All articles were related to colorectal cancer. Studies of vitamin B1 intake met the quality criteria (6–7 stars): four articles had seven stars, and three had six stars. The details of NOS are in Supplemental Online Material.
Fig. 2. A: The forest plots of all study. B: The forest plots of all study after sensitivity analysis. C: The forest plots of case-control. D: The forest plots of case-control after sensitivity analysis.
**Vitamin B1 Intake and the Risk of Colorectal Cancer**

**Association between vitamin intake and colorectal cancer**

All studies combined for roughly the same high dose level versus lowest categories of intake of vitamin B1 (thiamine) are in Fig. 2. Forest plots of all studies shown the pooled OR for vitamin B1 (thiamine) intake and colorectal cancer risk was 0.83 (95%CI, 0.72–0.96), with heterogeneity ($I^2=56.9\%$). We incorporated the results of case control studies. The results of case-control shown the pooled OR for vitamin B1 (thiamine) intake and colorectal cancer risk was 0.83 (95%CI, 0.71–0.96), with the heterogeneity ($I^2=63.9\%$). We also did a sensitivity analysis of all study. According to the results of sensitivity analysis, Key TJ’s study was removed. The final result was that there is a relationship between vitamin B1 (thiamine) and colorectal cancer with the heterogeneity ($I^2=16.3\%$). The pooled OR for vitamin B1 (thiamine) intake and colorectal cancer risk was 0.76 (95%CI, 0.65–0.89). We also did a sensitivity analysis of case-control studies. According to the results of sensitivity analysis, Key TJ’s study was removed. The final result was that there is a relationship between vitamin B1 (thiamine) and colorectal cancer with the heterogeneity ($I^2=29.1\%$). The pooled OR for vitamin B1 (thiamine) intake and colorectal cancer risk was 0.75 (95%CI, 0.64–0.89).

**Publication bias**

Begg and Egger’s tests were used to examine publication bias. With the Egger test, we found no evidence of publication bias for vitamin B1 (thiamine; $p=0.976$). With the Begg test, we found no evidence of publication bias for vitamin B1 (thiamine; $p=0.881$).

**DISCUSSION**

This meta-analysis evaluating the relationship between vitamin B1 and colorectal cancer. In this meta-analysis of epidemiological studies including 1 cohort studies and 6 case-control studies, we found vitamin B1 intake had an association with the incidence risk of colorectal cancer. Vitamin B1 intake is a protective factor in the incidence of colorectal cancer.

Some studies have shown that thiamine is associated with many cancers. Liu’s research concludes that thiamine transporter THTR2 gene expression is down-regulated in breast cancer (27). In subsequent studies, Liu et al. found that potential links between thiamine metabolism and genes may be involved in the oncogenesis of breast and lung cancer (28). A study supported the use of higher doses of thiamine to improve the treatment of cancer patients who have Wernicke’s encephalopathy (29). Experiments on animals had suggested that thiamin deficiency could be involved in colon carcinogenesis. They had found that the colons of rats fed diets marginally deficient in thiamin had an increased number of ACF (aberrant crypt foci) (30). A pilot randomized controlled trial found that the plasma thiamin concentrations of previous colonic polyps or intramucosal carcinomas were generally low compared to the reference range (31). Our study also demonstrated that vitamin B1 can prevent colorectal cancer. But, some of the cohorts studies shown none of the B-vitamins were associated with the risk of breast or colorectal cancers (26).

This meta-analysis has several strengths. First, this is the first meta-analysis evaluating the relationship between vitamin B1 intake and colorectal cancer. Additional strengths are the examination of the retrieved materials by at least two reviewers and strict evaluation standards. Our study has several limitations. First, as a meta-analysis of observational data, our results had recall and selection bias inherent in the original studies. Second, the adjusted factors differed in many studies and commonly included age, sex, energy, ethnicity, body mass index, physical activity, pack-years of smoking, family history of colorectal cancer, colorectal cancer screening, and intake of processed meat and alcohol. Finally, we used pooled RRs for roughly the same high dose level versus the lowest doses, but the definite dose differed slightly among studies. Given the limitation of this study, larger studies with a prospective design should be considered and investigated to validate the current findings.

Given the inadequacies discussed above, vitamin B1 intake is a protective factor in the incidence of colorectal cancer. But, well-designed multi-center trials with a larger sample size are needed to better demonstrate the association between Vitamin B1 intake and the risk of colorectal cancer.

**Authorship**

Yan Liu and Wenjing Xiong acquired the data, performed the literature review, and wrote the manuscript. Lei Wang acquired the data and contributed to the analysis data. Weiqing Rang and Yu Chuanhua evaluated the manuscript. Yan Liu and Wen-jing Xiong are the first co-authors.

**Disclosure of state of COI**

The authors declare that they have no competing interests.

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**Patient consent for publication**

Written informed consent was obtained for the publication of original data and materials.

**Supporting information**

Supplemental online material is available on J-STAGE.

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