

Analysis of the Impact of the Mediterranean Diet Pattern on Digestive System-related Cancers

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Abstract. Digestive system cancer is a cancer category with high incidence and mortality rates globally. Currently, commonly used treatment methods such as surgery, radiotherapy, and chemotherapy have drawbacks such as high cost and susceptibility to drug resistance and recurrence. Therefore, the positive role of dietary factors in the prevention and management of such cancers is gradually gaining attention. The Mediterranean diet, a traditional dietary pattern originating from countries along the Mediterranean coast, is centered on the high intake of olive oil, whole grains, vegetables, fruits, and legumes. It predominantly employs low-temperature cooking methods such as cold mixing and stewing to preserve nutrients. Existing research has shown that the Mediterranean diet has a protective effect on several common digestive system cancers, including gastric cancer, esophageal cancer, and colorectal cancer. The Mediterranean dietary pattern primarily functions by reducing the body's inflammatory response, minimizing oxidative damage to the body, and regulating the balance of gut microbiota. However, its effectiveness varies across different regions and gender groups. Currently, the Mediterranean diet faces challenges in practical application. Future research should focus on adapting this dietary pattern to different regional dietary habits and exploring its combined effects with other healthy lifestyles, thereby providing a more practical reference for the prevention and management of digestive system cancer.

Keywords: Mediterranean diet, meta-analysis, digestive system cancer, malignant tumor.

1. Introduction

Digestive system cancers, including malignant tumors such as colorectal cancer, gastric cancer, liver cancer, esophageal cancer, and pancreatic cancer, are among the cancer types with the highest incidence and mortality rates globally. According to data released by the National Cancer Center of China in 2022, digestive system cancers such as colorectal cancer, gastric cancer, and esophageal cancer ranked second, third, and sixth, respectively, in terms of new cases. For instance, in 2022, the number of new cases of colorectal cancer in China was approximately 517,100, with a death toll of about 240,000. The number of new cases of gastric cancer was around 358,700, with a death toll of about 260,400; the number of new cases of esophageal cancer was 224,000, with a death toll of 187,500 [1]. Currently, the main treatment methods for digestive system cancers include surgical resection, chemoradiotherapy, and targeted immunotherapy. However, these treatments face numerous challenges, such as high treatment costs, drug resistance and recurrence, and significant patient suffering [2]. Consequently, an increasing number of individuals are paying attention to the potential positive effects of dietary factors on digestive system cancers. Existing research has shown that dietary fiber and phytochemicals in the diet, through epigenetic regulation and apoptosis pathways, exhibit preventive potential against various digestive system cancers, including colorectal cancer. The Mediterranean Diet (MD) was first identified and proposed in the 1960s. It is a dietary pattern primarily consisting of plant-based foods, replacing refined carbohydrates with whole grain foods, supplemented by a rich variety of vegetables, legumes, fruits, nuts, and moderate amounts of poultry, eggs, dairy products, and seafood [3].

Numerous scholars, both domestically and internationally, have indicated that this dietary pattern possesses significant preventive potential against various digestive system tumors, including colorectal cancer, liver cancer, and esophageal cancer. Large cohort studies and meta-analyses have suggested that adhering to a Mediterranean diet can significantly reduce the risk of developing these cancers, and the protective effect may be more pronounced in males. The protective mechanisms

primarily involve multiple pathways, including anti-inflammatory effects, improved metabolism, regulation of gut microbiota, and influencing carcinogenic mediators. However, it is worth noting that the Mediterranean diet may not be beneficial for all cancer patients. Recent research has found that for certain specific cancer types, a high Mediterranean diet score may even lead to poor prognosis. This result suggests that dietary intervention needs to be personalized based on cancer type and individual differences, and cannot be generalized.

Although the Mediterranean Diet has garnered widespread attention in the field of digestive system health in recent years, and existing evidence supports its positive impacts, further research is still needed on specific implementation strategies and applicability to different populations. Currently, literatures are summarizing the research progress of MD on metabolic system-related cancers, yet there is a scarcity of reviews on MD's effects on digestive system cancers. Based on this, this article systematically summarizes the research progress and practical application value of the Mediterranean Diet pattern for digestive system-related cancers (gastric cancer, esophageal cancer, and colorectal cancer), providing a theoretical reference for treatment options of digestive system-related cancers.

2. Characteristics and Nutritional Value of the Mediterranean Diet

The Mediterranean Diet is a traditional dietary pattern originating from the Mediterranean coastal regions, widely prevalent in Mediterranean countries such as Greece, Spain, France, and southern Italy [4]. MD centers around the high intake of olive oil, whole grains, vegetables, fruits, and legumes, while advocating moderate consumption of fish, seafood, dairy products, and a small amount of eggs, as well as moderate alcohol consumption. Characterized by emphasizing the naturalness, freshness, and diversity of ingredients, the Mediterranean dietary pattern has received widespread attention in recent years.

The Mediterranean Diet has three typical characteristics. Firstly, MD uses extra-virgin olive oil as the main cooking oil, and its nutritional characteristics mainly include the following aspects. The energy supply ratio of fat is 25% to 35%, with a low intake of saturated fatty acids (7% to 8%) and a higher intake of unsaturated fatty acids, which helps to reduce cholesterol levels and reduce the risk of cancer [3]. Secondly, the dietary fiber intake in MD is significantly higher than that in the Western industrialized diet pattern, with a daily intake of whole grains, fresh fruits and vegetables, and legumes reaching more than 400 grams. These ingredients not only provide abundant vitamins and minerals but also offer a variety of phytochemicals. Furthermore, fish and poultry are the main protein sources in MD, with red meat intake limited to 1-2 times per week, and dairy products mainly consisting of fermented products (such as yogurt and cheese).

The Mediterranean Diet pattern advocates minimalist cooking, often utilizing low-temperature processing methods such as cold mixing and stewing, to maximize the retention of nutrients in ingredients. However, this pattern is not merely a simple dietary combination, but rather an overall health system encompassing lifestyle elements such as regular sleep and moderate exercise. Existing research has shown that the MD dietary system can effectively reduce the risk of cardiovascular diseases, improve metabolic health, inhibit the growth of cancer cells, and contribute to the development of the nervous system. It is widely regarded as an ideal dietary approach that is scientifically balanced and carries both cultural and health significance, laying the foundation for further exploration of its positive effects on digestive system cancers [5].

3. The Effect of the Mediterranean Diet Pattern on Digestive System Cancer

Existing research indicates that the pathogenesis of digestive system cancers is closely related to processes such as chronic inflammation, oxidative stress, and intestinal flora imbalance. The active components in the Mediterranean diet pattern may inhibit inflammatory responses by regulating signaling pathways such as Nuclear Factor kappa-B (NF- κ B), while blocking malignant transformation of epithelial cells by repairing Deoxyribonucleic Acid (DNA) damage and regulating

cell apoptosis [6]. Large-scale epidemiological evidence further shows that people who adhere to the Mediterranean diet for a long time exhibit a significant decrease in the incidence of diseases such as esophageal cancer and gastric cancer, suggesting that it may also have a certain attenuating effect on the incidence of colorectal cancer [7]. However, this protective effect shows significant heterogeneity across different regions, genders, and genetic backgrounds, and its specific mechanism of action remains to be systematically elucidated.

3.1. The Effect of Mediterranean Diet Pattern on Gastric Cancer

The association and mechanism between the Mediterranean Diet and the risk of gastric cancer have been analyzed through multiple systematic studies. Bai et al. employed a systematic review analysis method, integrating 11 studies with over 1.3 million samples and a cohort follow-up duration ranging from 11.0 to 20.3 years. They firstly clarified that the protective effect of MD on gastric cancer exhibits subtype and gender differences, with an overall risk reduction of 32% (pooled Odds Ratio (OR)=0.68, 95%, Confidence Interval (CI) 0.57–0.81, $P<0.001$). Both cardiac adenocarcinoma (OR=0.64) and non-cardiac adenocarcinoma (OR=0.68) showed significant reductions. The study proposed that the core mechanisms of MD in preventing gastric cancer are anti-inflammatory (i.e., inhibition of the NF- κ B pathway) and antioxidant (i.e., free radical scavenging effects of vitamins and carotenoids) [8].

An observational cross-sectional study involving 186 gastric cancer patients in Greece, with a median follow-up duration of 57 months, found that high adherence to Mediterranean diet could prolong patient survival. Specifically, the median survival time in the high adherence group was 102 months, significantly longer than that in the low adherence group (17 months, $P<0.0001$), confirming the protective effect of MD on gastric cancer survival. The study proposed that components such as polyphenols in MD can achieve anti-inflammatory, antioxidant, and activation of tumor suppressor genes such as p53, promoting cancer cell apoptosis and reducing the risk of gastric cancer [9].

In terms of geographical applicability, a study involving 172 gastric cancer patients and 314 healthy controls (case: control = 1:2) in Jordan was conducted for a period of 3 years without intervention, solely comparing the dietary pattern differences between cases and controls. The results indicated a significant correlation between the Mediterranean Diet and a reduced risk of gastric cancer: the OR for the fourth quartile was 0.212 (95% CI 0.107–0.419, $P < 0.05$), and the OR for the third quartile was 0.394 (95% CI 0.211–0.736, $P < 0.05$). At the statistical level, after adjusting for confounding factors such as age, gender, and smoking, the protective effect of the Mediterranean Diet pattern remained significant ($P < 0.05$), thus validating the preventive value of MD for gastric cancer in the Middle Eastern population for the first time. Additionally, the study found that dietary fiber provided by fresh fruits and vegetables in the Mediterranean Diet pattern can regulate intestinal flora, and hydroxytyrosol in olive oil can reduce gastric mucosal damage. Both mechanisms collectively reduce the risk of gastric cancer by decreasing oxidative stress and chronic inflammation [10].

3.2. The Effect of Mediterranean Diet Pattern on Esophageal Cancer

Esophageal cancer is one of the most prevalent malignant tumors of the digestive tract globally, ranking among the top in terms of incidence rate and mortality rate among malignant tumors, and exhibiting significant regional and pathological subtype differences. Clinically, esophageal cancer is mainly divided into two major pathological types: esophageal squamous cell carcinoma and esophageal adenocarcinoma, which differ significantly in terms of the location of onset, pathogenic factors, and pathological manifestations. Early symptoms of esophageal cancer are subtle and often overlooked. However, as the disease progresses to the middle and late stages, patients will experience typical progressive dysphagia, accompanied by symptoms such as persistent pain behind the sternum, hematemesis, or black stool.

Existing research has shown that the Mediterranean Diet is closely associated with the occurrence and development of esophageal cancer. A case-cohort study employing a Dutch cohort design, with 120,852 participants aged 55–69 at baseline, randomly selected 5,000 individuals to form a subcohort

and followed them for 20.3 years. Dietary intake in the year before baseline was assessed using 150 semi-quantitative food frequency questionnaires, and patients diagnosed with 133 cases of esophageal squamous cell carcinoma (ESCC) and 200 cases of esophageal adenocarcinoma (EAC) were analyzed. The study results revealed that for every 2-point increase in adherence to the Mediterranean Diet without Alcohol (aMEDr), the risk of ESCC in men significantly decreased by 43%, while there was no significant association in women. Additionally, it was found that compared to the lowest group (0-3 points), the highest group (6-8 points) of male aMEDr scores had a 65% reduced risk of ESCC, but no statistical association was observed for the risk of EAC. The conclusion indicated that among the Dutch population, a higher adherence to the Mediterranean Diet without Alcohol significantly reduces the risk of ESCC in men but does not provide protection against EAC; for women, a higher adherence to the Mediterranean Diet without Alcohol does not significantly protect against either ESCC or EAC. The study proposed that the mechanism by which the Mediterranean Diet pattern reduces the risk of ESCC may involve the high intake of fruits, vegetables, nuts, and whole grains, which provide antioxidant polyphenols and dietary fiber to reduce oxidative stress and inflammation, decrease the formation of N-nitroso compounds, and the low intake of red meat and processed meat, which reduces exposure to heme iron and carcinogens from high-temperature cooking. Meanwhile, the monounsaturated fats in olive oil and omega-3 fatty acids in fish may also synergistically reduce cancer risk through anti-inflammatory pathways [11].

Currently, although there have been many relevant research advancements in the application of the Mediterranean diet in improving chronic diseases such as cancer, there are relatively few research papers on its use in the field of esophageal cancer, and further experimental evidence is still needed to support its effectiveness.

3.3. The Effect of Mediterranean Diet Pattern on Colorectal Cancer

Existing evidence indicates that there is a certain association between the Mediterranean Diet and colorectal cancer (CRC), but its effect scenario and intensity vary depending on population characteristics. A prospective cohort study involving 35,372 middle-aged women in the United Kingdom (UK) assessed baseline dietary adherence using a 10-component Mediterranean Diet score, with a median follow-up of 17.4 years. The results showed that for every 2-point increase in MD score, the overall risk of CRC was significantly reduced by 12% (hazard ratio (HR) = 0.88, 95% confidence interval (CI): 0.78–0.99, P-trend = 0.03). Additionally, the study found that a high intake of legumes (≥ 73 g/d) reduced the risk of rectal cancer by 44% (HR = 0.56, 95% CI: 0.35–0.91, P = 0.017), revealing the differentiated effects of MD on CRC subtypes in non-Mediterranean populations. The study concluded that the Mediterranean Diet pattern is moderately and nonlinearly negatively associated with the risk of CRC in British women, and its protective effect on rectal cancer is significantly stronger than that on colon cancer. Possible mechanisms include: high dietary fiber diluting carcinogens, accelerating intestinal transit, and generating short-chain fatty acids; high fish intake providing omega-3 polyunsaturated fatty acids to inhibit pro-inflammatory prostaglandin E₂; low red meat and processed meat reducing exposure to heme iron, N-nitroso compounds, and polycyclic aromatic hydrocarbons, heterocyclic amines, and other carcinogens produced by high-temperature cooking; and the overall anti-inflammatory effect of the diet, improved insulin sensitivity, and regulation of gut microbiota may also collectively play a protective role [12].

Another controlled study involving 395 Moroccan CRC patients and matched controls over 15 months found that both moderate (OR=0.48, 95% CI: 0.37–0.69) and high (OR=0.39, 95% CI: 0.28–0.56) adherence to the modified Mediterranean Diet score, tailored to the religious and cultural background of the southern Mediterranean, significantly reduced the risk of CRC (P<0.001). This provides the first evidence for a culturally adapted MD assessment. Additionally, the study suggests that the preventive mechanism of MD for colorectal cancer may be due to the dietary fiber in MD being fermented by gut microbiota to produce short-chain fatty acids, which inhibit tumors, and polyphenols reducing chronic inflammation through antioxidant activity and inhibition of the NF- κ B

pathway. Furthermore, the dietary pattern influenced by the religious culture of the southern Mediterranean enhances this protective effect [13].

4. Conclusion

Existing research has confirmed that the Mediterranean diet pattern has a multi-level preventive effect on digestive system cancers. By systematically reviewing the epidemiological and mechanistic studies on esophageal cancer, gastric cancer, and colorectal cancer, it can be clearly established that this dietary pattern exerts protective effects primarily through mechanisms such as anti-inflammatory and antioxidant activities, regulation of gut microbiota, and blockade of malignant transformation signaling pathways. Among these, the regulatory effects of active ingredients such as polyphenols and monounsaturated fatty acids on key pathways like NF- κ B and Nuclear factor erythroid 2-related factor 2 (Nrf2) are particularly prominent.

Given the potential and complexity of the Mediterranean diet in the prevention and treatment of digestive system cancers, its application in clinical practice must emphasize the principle of individualization. For the general public and high-risk groups, it is recommended to adopt the Mediterranean diet as an effective primary prevention strategy. Advocating an increase in the intake of fruits and vegetables, whole grains, and high-quality fats such as olive oil, while reducing red meat and processed meat, can leverage their anti-inflammatory and antioxidant properties to reduce cancer risk, especially for men, where this protective effect may be more pronounced. However, for patients with confirmed cancer, during treatment, they often experience appetite loss, weakened digestive function, and immunosuppression. Blindly following a high-fiber, high-plant-based diet pattern may increase the burden on the gastrointestinal tract and even the risk of infection. Therefore, it is recommended to adapt the Mediterranean diet according to the varying conditions of patients, such as moderately refining dietary fiber, ensuring the hygiene and safety of ingredients, and closely monitoring nutritional status and treatment-related toxicity.

However, current clinical applications still face challenges, namely the difficulty in substituting core ingredients due to regional dietary cultural differences, such as the limited acceptance of olive oil in non-Mediterranean regions. Therefore, in future research, emphasis should be gradually placed on the localization and adaptation of the Mediterranean diet, systematically evaluating the feasibility and effectiveness of traditional dietary ingredient substitution schemes tailored to the dietary habits and disease spectrum characteristics of non-Mediterranean populations. At the same time, collaborative research on dietary intervention and other lifestyle factors should be strengthened, exploring the optimal implementation path within a medical framework. The advancement of these research directions will help elevate the Mediterranean diet from an experiential recommendation to a medical-based individualized prevention and treatment strategy, ultimately achieving a paradigm shift in digestive system health management.

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