

# Precision Nutrition in the Clinical Application of Digestive Tract Malignant Tumor Treatment: Current Status and Prospects

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**Abstract.** Digestive tract malignancies are a major public health problem in China. Currently, precision nutrition has gradually become a key intervention measure in its treatment. However, there are differences in the understanding of its concept and connotation in China and abroad, and clinical application and research are diverse. At present, precision nutrition has made certain progress in the three aspects of digestive tract tumor treatment. For example, research on nutrition assessment and dietary regulation has been carried out in colorectal cancer (CRC), personalized nutrition assessment and intervention timing have been explored in gastric cancer, and multi-omics applications and the effects of non-drug nutrition preparations have also been involved in esophageal cancer. However, there are still many shortcomings in the clinical application of precision nutrition in digestive tract tumors, such as the lack of popularization of individualized nutrition needs assessment, the gap between cost and technical feasibility, and so on. This article analyzes the research in these aspects and provides a new way to improve the nutritional status of patients and lay the foundation for personalized intervention. However, the application of the research at the system level and socioeconomic factors has not been fully explored. In the future, technological innovation, interdisciplinary cooperation, etc., should be emphasized on basic medical research and multidisciplinary integration to improve treatment effects and quality of life. At the same time, there are still problems to be solved, and subsequent research can be strengthened in related directions.

**Keywords:** Digestive tract malignancies, Precision nutrition, Clinical application, Nutritional assessment, Tumor treatment.

## 1. Introduction

Digestive tract malignancies are a major public health problem in China. The latest report in 2020 shows that gastric cancer (GC), esophageal cancer, and colorectal cancer (CRC) rank among the top three newly digestive tract tumors globally, with a total of over 3.623 million cases, and the mortality rates are all among the top 10 global malignant tumor mortality rates [1]. The situation in China is also like the global situation. Currently, as the resistance of digestive tract tumors to various chemoradiotherapy regimens is becoming increasingly serious, there is an urgent need to develop more cancer treatment directions. Many practices and studies have proved that the nutritional status of patients affects the prognosis and quality of life of patients. Precision nutrition is gradually becoming a key intervention measure, even the first-line clinical therapeutic method in the treatment of digestive tumors, it also becomes an effective anti-cancer tool. The incidence of malnutrition among malignant tumor inpatients in China is as high as 80%, and about 10% - 20% of tumor patients die of malnutrition rather than the tumor itself [2]. The metabolic abnormalities, intestinal microbiome destruction, and systemic inflammation caused by the tumor and its treatment directly affect the intake and absorption of nutrients. Especially in digestive tract tumors, the nutritional status is particularly prominent, and the postoperative nutritional status directly affects wound healing and infection risk.

With precision medicine being valued as one of China's national strategies in 2015, nutritional treatment has also entered the "precision era". Unlike traditional nutritional treatment, precision nutrition comprehensively considers various aspects of individual genetic background, environmental factors, physiological metabolism, disease prognosis, etc. to provide targeted treatment plans [3], and

has shown outstanding effects in the nutritional treatment of tumors. However, at present, experts at home and abroad do not have a consistent understanding of the concept and connotation of precision nutrition, and the application and research of precision nutrition in clinical practice are also diverse. Based on this background, this article will combine the clinical application and research status of precision nutrition treatment for common digestive tract malignant tumors, such as CRC, GC, and esophageal cancer. It will reflect on the deficiencies and prospects of precision nutrition in the treatment of digestive tract malignant tumors, and strive to achieve an effective personalized intervention scheme to improve the clinical outcome of patients with digestive tract tumors and enhance the overall treatment level.

## 2. Concept of Precision Nutrition

Precision nutrition refers to a customized nutritional intervention strategy based on an individual's genetic characteristics, metabolic status, and lifestyle. Its core lies in optimizing personal health status through scientific nutrient intake regulation, especially showing significant effects in disease treatment.

The guidelines for precision nutrition developed by the International Society of Nutrigenetics & Nutrigenomics (ISNN) in 2016 categorize precision nutrition into three levels: traditional nutrition based on diagnosis and treatment guidelines for specific populations, individualized nutrition based on an individual's nutrient-related phenotypic characteristics, and gene-oriented nutrition guided by rare or common gene variants.

By analyzing the published literature from 2016 to 2024, the term "precision nutrition" is often associated with metabolomics and nutrigenomics studies in foreign literature, which is defined as using omics technologies to evaluate an individual's response to specific foods or dietary patterns and determining the most effective interventions at the molecular level by assessing such responses to improve diet or lifestyle, thereby promoting health, preventing and treating specific diseases. Meanwhile the term "precision nutrition" in domestic literature often refers to the concept of "individualized nutrition," which is based on the traditional nutritional assessment and primarily involves analyzing individual patients' clinical characteristics and health data using multiple disciplinary technologies, and then providing targeted and differentiated clinical nutrition interventions, which falls within the realm of clinical practice.

## 3. Application of Precision Nutrition in the Treatment of Digestive Tract Tumors

In line with the guidelines formulated by the ISNN, the application of precision nutrition in the treatment of digestive tract tumors is also reflected in three levels [4].

First, traditional nutritional support is still the main approach. Global clinical nutrition academic organizations have issued related guidelines and consensus, proposing standardized diagnostic and treatment strategies for nutritional support. Nutrition or dietary guidelines have undergone years of modifications from the population level to the level of specific diseases, reflecting the development of precision nutritional support.

Second, the research on individualized nutritional support is booming. It includes providing personalized nutritional support for patients from multiple dimensions and channels such as multidisciplinary nutritional support teams, whole-course nutritional management, and computer artificial intelligence systems, from nutritional assessment to nutritional education and nutritional follow-up monitoring.

Third, the research on nutritional support based on genotype characteristics is flourishing. Research and application are carried out from multiple angles, from studying the relationship between the body's metabolomics and tumors to studying the changes of related target genes and biomarkers

in the occurrence and course of tumors, and from the research of mechanisms to the research and development of nutritional products in the whole industry chain [5].

### 3.1. CRC

Existing studies have shown that CRC patients should undergo nutritional assessment through the Nutritional Risk Screening 2002 (NRS 2002) and the Patient-Generated Subjective Global Assessment (PG-SGA). A multicenter, retrospective, observational cohort study included patients with CRC and GC (GC) who underwent radical surgery, and finally verified a nomogram prediction model based on the NRS 2002 score for predicting the overall survival of patients with gastric and CRC after surgery. The model has good discrimination, calibration, and clinical practicability in predicting the long-term survival rate of patients with gastrointestinal cancer after radical resection [6], and can also be used for survival prediction. Additionally, some studies have used the indirect calorimetry method as the gold standard to evaluate the daily energy consumption of patients [7] or personalized adjustment of nutritional intervention strategies under the guidance of assessment scales can effectively improve their nutritional status [8-10].

Diet is a powerful regulator of many axes involved in cancer, especially in digestive tract tumors, including growth signaling, immunity, and the microbiome [11]. For example, current nutritional treatment recommends using vegetable oil as the main cooking oil, with a daily oil amount controlled within 10 grams, and encourages the increase in the intake of high-fiber foods such as apples, celery, and oats. These measures help reduce the risk of colon cancer by improving the intestinal microenvironment and promoting intestinal peristalsis.

Many studies have confirmed the negative correlation between the Mediterranean diet and the risk of CRC onset. In 2020, a meta-analysis (prospective cohort studies  $n=13$ ) found that the incidence of colon cancer in subjects with low adherence to the Mediterranean diet was 13% higher than that in subjects with high adherence. Schulpen M et al. found that adhering to the Mediterranean diet for nearly 18 years after following 35,372 middle-aged women helps reduce the risk of colon cancer [12]. The mechanism may be that olive oil polyphenols and other substances inhibit the expression of colon inflammatory factors, improve and regulate the intestinal microenvironment, thereby reducing the risk of occurrence. There are also some preclinical studies that have discovered the effects and action mechanisms of Mediterranean diet components on cancer cells and possible preventive mechanisms [13]. Clinicians can also recommend this lifestyle to patients and supplement it with food and plant therapeutic compounds, which may be the future research direction [5].

In addition, some studies have elucidated the impact of a certain type of substance on CRC, thus providing a basis for the choice of diet. Basic research conducted by Columbia University found that *Fusobacterium nucleatum* plays an accelerating role in the growth of CRC, revealing the potential impact of the gut microbiome on tumor progression, and to a certain extent suggesting the potential of optimizing the gut flora through diet adjustment in the prevention and treatment of CRC [14]. The CYP class eicosatetraenoic acid pathway mediates the promoting effect of dietary linoleic acid on colon cancer [15], and nano-peroxidase is a promising anti-inflammatory and antibacterial agent that can combat bacteria and inflammation associated with CRC [16]. A mouse model experiment of colon cancer found that azoxymethane/dextran sulfate sodium treatment can lead to an increase in epoxy fatty acid levels, and cytochrome P450 monooxygenase plays a key role in this process. It reveals the role of metabolic pathways in the development of colon cancer and provides a new theoretical basis for precision nutritional intervention [17].

The role of precision nutrition in the clinical application of CRC is becoming increasingly prominent. These research results, from the macro-level suggestions on the implementation methods of precision nutrition to the explanation of pathological mechanisms at the molecular level, provide empirical support for precision nutrition treatment. In the future, more close interdisciplinary cooperation, continuous research investment, and continuous optimization of clinical practice are needed to bring new breakthroughs to the nutritional treatment of CRC.

### 3.2. GC

There is a close relationship between GC and gastric microbiota. *Helicobacter pylori* is widely recognized as a predisposing factor for GC, but there is increasing evidence of diverse changes in the gastric microbiota during the development of GC, such as the enrichment of bacteria such as *Streptococcus* and *Clostridium* in GC tissues, and the pathogenic bacteria *Streptococcus pharyngiophthisis* and the EBV promoting gastric tumorigenesis. Therefore oral, gastric mucosa and intestinal microbiota have full potential as diagnostic markers [18].

Several studies have been conducted on the comparison of different nutritional assessment methods in detecting malnutrition in GC patients to explore the strengths, weaknesses and relevance of, for example, NRS2002, MUST, MST, PG-SGA, MNA, etc., and a number of studies consistently show that there are limitations in any single assessment method or tool and in accurately measuring the nutritional status irrespective of the objective nutritional parameters or the subjective evaluation [19]. Therefore, individualized nutritional assessment should be carried out with a view to more accurately assessing the nutritional status of patients. Researchers have attempted to develop more reliable evaluation systems for combinations of biochemical factors to identify patients with poor nutritional status, such as the Prognostic Nutritional Index (PNI), the Douglas Prognostic Score, and so on [20]. In the evaluation of physical factors, in addition to body weight and BMI, in recent years, researchers have become increasingly interested in the assessment of body composition in GC patients, which may be related to the discovery of the link between sarcopenia and surgical outcomes in patients [21].

Optimization of the timing of nutritional interventions is one of the embodiments of precision nutrition: the optimal timing of nutritional interventions in different phases is clearly defined, including preoperative nutrition, postoperative nutrition, and progression nutrition. In the preoperative nutritional intervention phase, both ASPEN and ESPEN guidelines recommend enteral nutritional feeding whenever possible. Successful studies on the frequent application of immunonutrition in enteral nutritional formulations, such as the use of arginine and omega-3 fatty acids, can enhance the patient's immune level. However, the actual utility of preoperative use of immunoglobulin is still controversial [20]. And early initiation of ON or EN is recommended in postoperative nutritional interventions, which is related to the recommendations of ERAS. In overall progressive nutrition, it is more effective to establish a nutritional support team and manage patients in a multidisciplinary manner than for team members to act independently [20].

With the maturation of new technologies such as gene, protein, metabolism, and microbiomics, precision nutrition in GC is also available at the level of individual genetic background level, metabolic profile, gut microbiome profile, lifestyle, and physiological status. Nutrigenomics attempts to reveal diet-related risk genes on a genome-wide scale, e.g., red meat and its processed products may promote GC due to the promotion of endogenous NOC formation by heme iron and thus inducing P53 mutations, and the products of dietary fiber play an anticancer role by suppressing the expression of genes such as CCNA2[22]. Immunomicroecological nutrition has also been widely used in clinical practice in recent years, for example, adding probiotics such as *Lactobacillus* and *Bifidobacterium* to enteral nutritional formulations to counteract the effects of *Helicobacter pylori* or utilizing short-chain fatty acid-producing flora to enhance therapeutic efficacy of GC and attenuate the associated adverse events [18]. Certain specific nutrient changes occur in oncology patients, for example, stored iron is negatively correlated with the risk of GC [22], but impaired iron absorption is the main cause of iron-deficiency anemia after gastrectomy [23], and targeted nutrient supplementation and novel nutritional agents, as well as the timing of their application, is one of the research priorities in precision nutrition.

Despite the great progress in clinical nutritional therapy, the role of neoadjuvant therapy and perioperative nutritional support in GC patients remains to be determined.

### 3.3. Esophageal cancer

Esophageal cancer is a common malignant tumor of the gastrointestinal tract, and its pathogenesis is related to a variety of factors in the tumor microenvironment. In 2019, Zheng Junqiong et al. found

in their study that the level of mitochondrial localization of TIGAR proteins in esophageal cancer cells is closely related to the radiosensitivity of the cells. By interfering or overexpressing TIGAR protein, the level of oxidative stress and autophagy in esophageal cancer cells can be effectively altered, which in turn affects the radiosensitivity of cells [24]. This finding provides a new theoretical basis for radiation therapy of esophageal cancer and a new direction for the application of precision nutrition in esophageal cancer treatment. In addition, the effect of adipose tissue on malignant fluid and the application of ketogenic fat reduction method was pointed out in the 2017 Electronic Journal of Oncology Metabolism and Nutrition, which provided a new perspective for precision nutrition therapy, which indicated that by adjusting the state of adipose tissue and the metabolic environment, tumor drug resistance and therapeutic effects could be improved [25].

In the treatment of digestive tumors, the application of precision nutrition gradually shows its clinical value, especially in the treatment of esophageal cancer. In 2015, Xia Yuhan et al. for the first time applied non-pharmacological nutritional preparation (FSMP) for early enteral nutrition (EEN) after esophageal cancer surgery in the region. The study showed that FSMP effectively accelerated the recovery of gastrointestinal function of patients, which not only could shorten the hospitalization time, but also reduce the medical cost, and improve the quality of postoperative recovery of patients for the precise nutritional management of patients in the perioperative period [26]. In 2021 Zhang Jianping and Chen Yan et al., through comparative study, found that the integrated intervention combining dietary care and nutritional support could effectively improve the patient's satisfaction with the nursing care and the comprehensive ability scores, providing a valuable reference for future clinical practice and research [27].

In recent years, the application of multi-omics research in esophageal cancer and its precise nutrition has been gradually deepened, providing an important basis for individualized nutritional interventions. In 2020, Wu Lei's study proposed a method combining generative adversarial networks and deep convolutional neural networks for optimizing imaging diagnosis of esophageal cancer [28]. This study improved the accuracy of predicting preoperative staging and lymph node metastasis status of esophageal cancer through the fusion of multi-omics information, which provided data support for the development of precision nutritional protocols and pushed forward the advancement of personalized treatment. In 2023, Xiumarium Shen, Yan Li, and Lili Shi showed that the combination of multi-omics enabled precision nutrition to be based not only on traditional nutritional assessment techniques, but also on the use of high-throughput data analysis to develop new nutritional intervention tools [29]. It was found that the application of multi-omics technology in the field of precision nutrition provides more comprehensive and fine-grained data support for individualized nutritional interventions, which is of great clinical significance for the treatment and management of digestive system tumors.

Although precision nutrition shows potential in the treatment of esophageal cancer, there are still research shortcomings. First, although the use of FSMP in early postoperative enteral nutrition has been shown to accelerate recovery, the long-term efficacy and applicability to different patient subgroups have not been clarified. Second, current studies have focused on short-term outcomes and lacked systematic assessment of long-term nutritional management and quality of survival. In addition, although comprehensive dietary care has improved patient satisfaction, how to individualize nutritional interventions more precisely still needs to be explored. Finally, studies on the interaction between nutritional interventions and the esophageal cancer microenvironment are insufficient, thus limiting the full application of precision nutritional strategies.

Looking forward, this article suggests that the integration and analysis of multi-omics data should be strengthened to enhance data processing and interpretation capabilities, so that the results of genomics, metabolomics and microbiomics can be more effectively applied to individualized nutritional interventions. As for research, it should focus on clinical trials to verify the actual effects and safety of precision nutritional interventions for patients with digestive tumors. In addition, artificial intelligence and machine learning technologies should be combined to analyze multi-omics

data and apply them to clinical decision-making, which is expected to bring new opportunities for the development of precision nutrition.

#### **4. Insufficient and Prospective Clinical Application of Precision Nutrition in Gastrointestinal Tumors**

Although precision nutrition has made some progress in the treatment of digestive tract tumors, it still faces many challenges.

##### **4.1. Individualized Nutritional Needs Assessment is not yet Fully Popularized**

Current nutritional screening and assessment scales are usually generalized, resulting in nutritional intervention protocols that may fail to adequately target patients' specific pathological and metabolic characteristics. Further development of individualized nutritional assessment techniques, combined with metabolomics and genomics, is needed to provide more precise nutritional intervention protocols to address the specific needs of different patients. In addition, early nutritional interventions have time constraints and resource limitations in practice, which affect the effectiveness of the interventions. How to effectively integrate precision nutrition with traditional treatment modalities is also a key issue in current research.

##### **4.2. Cost of Precision Nutrition and Feasibility Gap of Technology Implementation**

For example, the use of indirect calorimetry to assess the level of energy consumption of patients is certainly accurate and can get better nutritional intervention results, but due to the complexity of its methodology, the conditions of use are severely restricted and cannot be promoted. The process of implementing precision nutritional management also significantly increases hospital labor costs and makes implementation at the grassroots level difficult, which also requires high-quality research to determine its cost-effectiveness. In addition, although artificial intelligence-managed nutritional meal boxes help to improve the efficiency of nutritional supervision, their application is still in the exploratory stage, and the cost and feasibility of technology implementation need to be further evaluated.

##### **4.3. Disconnect between Experimental Research and Clinical Application**

Experimental research focuses on the elaboration of mechanisms, but there is no good clinical application practice. Clinical practice often favors "nutritional management", and the two are not well connected. Clinical patients have variable disease and metabolic status, and more research design and analysis methods are needed to assess the efficacy of experimental studies applied to individualized nutritional interventions. Clinical trials and multidisciplinary cooperation should also be strengthened to explore the optimal combination of precision nutrition and other therapeutic means to enhance the comprehensive treatment effect and quality of life of digestive tumor patients.

##### **4.4. Nutritional cognition of Patients and Healthcare Personnel Needs to be Improved**

At present, the level of nutritional cognition of hospitalized patients is low, and at the same time, this phenomenon is also related to the low level of nutritional cognition of healthcare personnel [30, 31]. At present, the nutritional knowledge of health care personnel and patients has a single way of acquisition, and there are fewer cognitive assessment tools, and the limitations of the cognitive level affect the performance of nutritional interventions by health care personnel and the compliance of patients, thus affecting the results of nutritional interventions. Improving the level of nutritional knowledge of healthcare personnel and patients can also improve the level of clinical application of precision nutrition.

#### 4.5. Weak Application of Big Data Analysis

Although some studies have begun to apply Internet platforms, portable wearable devices, etc. to record or track patients' nutritional status data and carry out relevant data analysis, the interaction between studies is poor, there is no broader organizational coordination, the data samples are usually small, and the results of the study are relatively one-sided. More and broader big data are needed for validation.

### 5. Conclusion

In recent years, research on the clinical application of precision nutrition has made progress both at the molecular level and at the macro level. In the treatment of digestive tract malignancies, customized intervention strategies based on individual conditions have been important in the treatment of colorectal cancer, gastric cancer, and esophageal cancer. Its significance lies in providing new ways to improve patients' nutritional status, prognosis, and quality of life, and laying the foundation for personalized intervention. However, the limitations of current research are also obvious, the research depth, cognitive popularity, and practicality of precision nutrition in the clinical application of digestive tract malignancies are not mature enough.

From the perspective of systems biology, the nutritional status of cancer patients is a complex biological system problem. When analyzing precision nutrition, this article focuses relatively on the individual research results of each part, and has not fully involved how to understand and apply precision nutrition from a system level to achieve the optimization of the overall treatment effect; this article also does not discuss in detail socioeconomic factors and sustainable development models.

The clinical application of precision nutrition requires the addition of more detection technologies, multi-omics fusion technology innovations, and the realization of interdisciplinary cooperation. At the same time, it is also necessary to focus on talent training, the improvement of social cognition, and the support of policies. In the clinical application of gastrointestinal tumors, basic medical research cannot be relaxed. Nutritional therapy should be based on tumor biological intervention, full-process treatment management and multidisciplinary integrated application to improve treatment effects and patient quality of life.

### Authors Contribution

All the authors contributed equally and their names were listed in alphabetical order.

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