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Application status and research progress of PRO in clinical tumor

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Abstract: Previous literature mainly focused on the application status of patient-reported outcomes in various medical fields and the research progress of PRO measurement tools at home and abroad. However, there is a lack of summary on the clinical research and practical application of PRO in gastrointestinal tumors. In view of this, this paper aims to discuss the application status and research progress of PRO in the clinical treatment practice of gastrointestinal tumors, in order to provide useful reference for future related studies.

1. Introduction

According to the global Cancer statistics in 2020, the incidence of colorectal cancer and gastric cancer in China ranks second and third respectively [1]. Chemotherapy is the main treatment for gastrointestinal tumors [2, 3]. The use of chemotherapy drugs has improved the survival rate of cancer patients, but chemotherapy-related toxic and side effects can reduce the quality of life of patients and even affect their survival. The actual toxicity symptoms of patients caused by chemotherapy, such as nausea, vomiting, constipation and anorexia, are more serious than those assessed by doctors, especially the toxicity rate reported by doctors after discharge is always lower than that reported by patients [4]. The traditional symptom management mode is reactive, usually the side effect symptom management of patients mainly depends on routine ward rounds or hospital visits. Especially in the interval between chemotherapy treatments, clinicians often fail to reliably monitor patients' symptoms and often underestimate their severity. As the side effects of chemotherapy of patients are not actively monitored and fully paid attention to, toxic side effects significantly reduce the efficacy of anti-cancer treatment and the quality of life of patients [5]. Patient-centered intervention can improve the quality of life and even survival rate of cancer patients, and the clinical application of patient-reported outcomes (PRO) is crucial to benefit patients with clinical gastrointestinal tumors [6]. This article reviews the application progress of PRO in clinical studies of gastrointestinal tumors, aiming to provide reference for future related studies.

2. Definition of PRO

In the early 2000s, the acronym "PRO" began to appear in research papers, and the European Medicines Agency (EMA) defined PRO as any outcome directly assessed by the patient himself, based on the patient's perception of the disease and its treatment [7]. In 2006, the food and drug administration (FDA) published *Industry Guidelines for Measuring Patient-Reported Outcomes*, which defined PRO in much the same way as the EMA, any report directly from a patient about the patient's own health. Not the subjective perception of the clinician. In other words, PRO is a patient's report of their actual health, not a clinician's subjective perception. PRO includes five core types, including disease-related symptoms, symptomatic adverse events, summative assessment of overall adverse reactions, and physical functions and role functions, which reflect patients' health status, symptoms, functions, satisfaction, health behaviors and quality of life. It is a multidimensional and subjective measurement standard, standardized and objectively quantified [8].

1) Gastrointestinal tumor PRO measurement tool

The toxicity rates reported by patients differ from those reported by physicians due to differences in the concealment of toxic symptoms and the ability of patients to express them. The use of standardized patient-reported outcomes measures (PROM) can normalize the collection of reported results of patients' perceptions of the disease and its treatment, which can help physicians comprehensively assess patients' health status and timely identify existing or potential problems. Doctors need to have a deep understanding of the patient's condition and needs to develop a more effective treatment plan[9]. PRO can be recorded in electronic or paper form, and the commonly used universal scale includes the Functional Assessment of Cancer Therapy, patient-reported outcomes version of the common terminology criteria for adverse events, Patient-reported outcomes version of the common Terminology Criteria for adverse events, PRO-CTCAE), the European QLQ(Quality of Life Questionnaire) series, and patient-reported outcomes measurement information system, PROMIS), etc. Functional Assessment of Cancer Therapy-Gastric, Functional Assessment of Cancer Therapy-Gastric, FACT-Ga, European Organization for Research and Treatment of Cancer Quality of Life Questiony-stomach 22, EORTC QLQ-STO22), etc. Currently, QLQ-STO22 is one of the most common tools for evaluating the quality of life of gastric cancer patients. It can be used to evaluate the therapeutic effect and life satisfaction of patients with different types and stages of gastrointestinal tumors [10].

3. The application of PRO in the field of gastrointestinal tumors

1) Symptom management and improvement of patients' quality of life: Anorexia, nausea, vomiting, constipation and diarrhea are common toxic symptoms of patients with gastrointestinal tumors in clinical treatment. With the enhancement of health awareness and nursing needs of clinical patients, delaying the progression of cancer patients and prolonging their survival period are no longer the only clinical goals to pursue, and reducing toxic symptoms and improving quality of life have gradually become the basic needs of cancer patients. Implementation of PRO in the academic practice of oncology has been shown to reduce emergency department visits and hospitalizations, extend patient tolerance to chemotherapy, and improve overall survival (OS) [11]. It is widely believed in the world that the application of PRO can benefit tumor patients in clinical treatment, and the application of PRO in routine clinical tumor treatment to evaluate the HRQoL of patients with gastrointestinal tumors, including related symptoms and functional status in HRQoL, is conducive to providing patients with effective and high-quality tumor care, routine evaluation of efficacy and improvement of patients' quality of life [12]. In 2021, Thierry Andre et al. published an open-label randomized Phase 3 trial, conducted at 192 cancer centers in 23 countries, that randomly assigned eligible patients with colon tumors to an equally proportional concentration. Patients were

given 200 mg of intravenous pembrolizumab or investigator-selected mFOLFOX6 chemotherapy regimen or FOLFIRI chemotherapy regimen per cycle, and their quality of life was quantified by item scores on the EORTC scale. The results showed that the EORTC QLQ-C30 symptom score was generally improved in the ptomlizumab group. Some patients who received pembrolizumab had a lower burden of treatment-related toxic symptoms, including nausea, vomiting, decreased appetite, and fatigue, than patients who received chemotherapy, and these symptom scores were generally higher in the chemotherapy group [13].

2) Clinicians provide important information for clinical decision-making: At present, there are many studies on the application of PRO in the gastrointestinal tract in foreign countries. Besides mainly for drug evaluation, PRO has also achieved good application effects in clinical trial efficacy evaluation and other aspects [14]. Often, information about toxic symptoms caused by chemotherapy in patients with GI tumors is not based on direct patient reports, but on reports from clinicians and caregivers in clinical trials, which greatly increases the potential for underreporting. Previous studies have shown that the toxicity rate reported by patients after using PRO is always higher than that reported by doctors [15]. PRO measurements provide valid, precise and reliable data quantifying the patient's perception of the disease and the impact of its treatment, taking into account the severity of the patient's disease, the impact of symptoms, the intensity of toxic side effects, and the level of annoyance. In the clinical treatment of gastrointestinal tumors, the routine integration of PRO data by healthcare professionals and the patient's participation in the disease process have a decisive impact on the prognosis of patients with gastrointestinal tumors, understanding the risks and benefits of proposed treatments, and weighing the impact of symptoms, functional status, and quality of life on life expectancy [16]. PRO data include objective physiological indicators of disease activity, which can be used to monitor the development trajectory of the disease, determine the severity of the disease, adjust the treatment plan suitable for the disease, and provide important information for treatment decisions of patients with gastrointestinal tumors [17].

3) Assessment of nutritional status: Abnormal digestive system in patients with gastrointestinal tumors leads to insufficient nutritional intake. In addition, long-term consumption of patients with malignant tumors and tumor treatment will also lead to malnutrition in patients, thereby increasing the incidence of tumor complications, reducing the quality of life of patients and even affecting their prognosis [18]. In one study, Guo Zhiqiang et al. assessed the nutritional status of 2 322 inpatients with gastric tumor by subjective global evaluation of patients, and analyzed the influence of nutritional status on the quality of life of patients. The quality of life of all patients was assessed according to the PRO data collected with the EORTC QLQ-C30 scale. The results showed that there were statistically significant differences in the quality of life of patients with different nutritional status, and malnutrition reduced the quality of life of cancer patients. The subjective holistic assessment of patients is worthy of clinical promotion and application, and it is recommended that clinical nutrition evaluation methods be adopted as soon as possible to assess the nutritional status of patients, and timely reasonable nutritional intervention be given [19]. In terms of diet, different dietary factors are closely associated with a higher risk of gastrointestinal tumors. Previous studies have pointed out that higher dietary folic acid intake is associated with a lower risk of gastric cancer and colorectal cancer [20]. Gonzalez-Palacios S et al., based on 11 studies included in the StoP Consortium that provided complete information on dietary folic acid intake, evaluated the role of major factors in the etiology of gastric cancer through pooled analysis of individual-level data. Each participant's dietary status was assessed using a country-specific food frequency questionnaire. The results show that there is a protective association between dietary folic acid intake and the risk of gastric cancer, and excessive alcohol consumption will lose the protective association between folic acid intake and cancer patients. Nutritional assessment and appropriate nutritional support are

crucial in the clinical treatment of patients with gastrointestinal cancer [21].

4) Healthcare providers enhance patient compliance: Understanding the actual needs of patients is the key to the implementation of PRO, and the application of PRO can provide useful information for the implementation of clinical trials and personalized care, thereby supporting the improvement of personal care experience of gastrointestinal patients in the clinical treatment environment, meeting the diversified needs of patients, and improving the quality of clinical cancer care and patient satisfaction [22]. PRO usually plays an auxiliary role in the treatment of gastrointestinal tumors, mainly allowing patients to perform non-invasive behaviors and command activities to perform relevant measurements [23]. The assessment in the functional areas of patients with gastrointestinal tumors, such as the assessment of some symptoms in the physiological function or the assessment of nutritional status, is more reliable, simpler and less costly than the subjective report. Compared with other clinical auxiliary examinations, it is less harmful to patients and greatly improves the treatment compliance of patients. A randomized controlled trial comparing the effects of PRO out-of-hospital follow-up provided by Clinical Nurse Specialists (CNS) versus traditional hospital routine management in patients with solid tumors found that: All participants expressed a preference for patient-reported outcome-based follow-up management, which could improve patient self-management satisfaction and treatment compliance at the appropriate time point, thereby improving patient clinical outcomes [24]. Although this study mainly focused on patients with endometrial cancer, it also has important implications for the clinical treatment of patients with gastrointestinal tumors.

4. Summary and prospect

In the early identification of patients who need attention or intervention, especially in the assessment of patients' mental health and social health, the application of PRO shows unique advantages and has a good evaluation effect. Continuous out-of-hospital follow-up based on PRO can combine outcome measures assessed by health care providers with subjective and objective patient measurements to more comprehensively assess changes in functional status and quality of life in patients with gastrointestinal tumors, helping health care providers make further clinical decisions. In view of the important application value of PROM in the field of tumor, how to integrate and even promote it to clinical tumor practice to more accurately evaluate the changes in symptoms, function and quality of life of patients during the whole course of treatment, improve the treatment experience and effect of patients, and further improve the treatment compliance of patients remains to be further discussed.

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